QUETIAPINE

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=> d his

     (FILE 'HOME' ENTERED AT 18:35:32 ON 08 MAR 2005)

     FILE 'REGISTRY' ENTERED AT 18:35:47 ON 08 MAR 2005
                E QUETIAPINE/CN
L1             2 S E3-5

     FILE 'CAPLUS' ENTERED AT 18:36:28 ON 08 MAR 2005
L2           453 S L1

     FILE 'REGISTRY' ENTERED AT 18:36:59 ON 08 MAR 2005
L3             1 S QUETIAPINE FUMARATE/CN
L4             1 S QUETIAPINE HEMIFUMARATE/CN

     FILE 'CAPLUS' ENTERED AT 18:37:19 ON 08 MAR 2005
L5           103 S L3
L6           103 S L4
L7           103 S L5 AND L6
L8             2 S CRYSTALLINE/IT AND L7
L9             3 S CRYSTALLINE AND L7
L10            3 S L8 OR L9

     FILE 'REGISTRY' ENTERED AT 18:38:55 ON 08 MAR 2005
L11       101507 S 6-6-7/SZ
L12      1366684 S C4N2/EA
L13        14544 S L11 AND L12
L14            3 S 11-PIPERAZIN? AND L13
L15         2466 S C6-C6-C5NS/EA
L16          405 S L12 AND L15

     FILE 'CAPLUS' ENTERED AT 18:41:19 ON 08 MAR 2005
L17          677 S L16
L18          103 S L7 AND L17

     FILE 'REGISTRY' ENTERED AT 18:41:40 ON 08 MAR 2005
L19        15445 S CHLOROETHOXY
L20       218556 S ETHANOL
L21          215 S L19 AND L20

     FILE 'CAPLUS' ENTERED AT 18:42:33 ON 08 MAR 2005
L22            3 S L18 AND L21
L23            6 S L10 OR L22

=> d ibib abs hitstr 1-6
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QUETIAPINE

L23 ANSWER 1 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:740310 CAPLUS
DOCUMENT NUMBER: 141:260785
TITLE: Synthesis of quetiapine and pharmaceutically acceptable salts thereof
INVENTOR(S): Diller, Dov; Dolitzky, Ben-zion
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004076431	A1	20040910	WO 2004-US5448	20040223
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004220400	A1	20041104	US 2004-785244	20040223
EP 1495008	A1	20050112	EP 2004-713790	20040223
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.: US 2003-448934P P 20030222
WO 2004-US5448 W 20040223

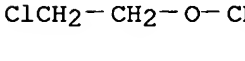
OTHER SOURCE(S): CASREACT 141:260785

AB Disclosed is a process for preparing quetiapine or its acid addition salt, in particular quetiapine hemifumarate comprising the step of reacting 11-piperazinyldibenzo[b,j][1,4]thiazepine hydrochloride and 2-(2-chloroethoxy)ethanol in a solvent in the presence of a base, and a phase transfer catalyst. The reaction is carried out at reflux temperature in the presence of alkali metal halide (preferably sodium iodide) which is optional, and the phase transfer catalyst selected from tetrabutylammonium bromide (TBAB), triethylbenzylammonium chloride, tricetylmethylammonium chloride, and tetrabutylammonium hydroxide (preferably TBAB) in a lower alkanol, an aromatic hydrocarbon, or dipolar aprotic solvent, or mixture thereof (preferably n-butanol, toluene, or DMF). Thus, 1-piperazinyl dibenzo [b,j][1,4]thiazepine hydrochloride (16.5 g, 44 mmol), 2-(2-Chloroethoxy)ethanol (7.2 g, 58 mmol) Na2CO3 (28.5 g, 270 mmol), NaI (270 mg, 0.18 mmol), TBAB (3 g), and toluene (82.5 mL) were charged to a round-bottomed flask equipped with a magnetic stirrer and a condenser with a calcium chloride drying tube. The flask and contents were heated in an oil bath at 105° under gentle reflux for 24 h. A Dean Stark trap was attached to the flask and the azeotropic mixture of water and toluene was distilled out. The product remaining in the flask was filtered-off and the precipitate (salts) was washed on the Buchner filter with small portions of toluene. To the combined filtrate and washings contained in a flask was added fumaric acid (2.6 g, 22 mmol) and the mixture was heated to boiling on a heating bath and then was removed from the heating bath, allowed to cool with stirring, and cooled in an ice bath and the contents filtered. The

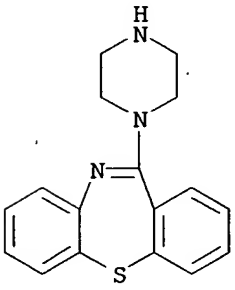
collected solid was recrystd. from 150 mL ethanol to give quetiapine hemifumarate (yield 14.0 g, 72 %).

IT **628-89-7**, 2-(2-Chloroethoxy)ethanol **753475-15-9**
RL: RCT (Reactant); RACT (Reactant or reagent)
(preparation of quetiapine or its salts by alkylation of piperazinyldibenzo[b,j][1,4]thiazepine hydrochloride with (chloroethoxy)ethanol in presence of phase transfer catalyst and base)

RN 628-89-7 CAPLUS
CN Ethanol, 2-(2-chloroethoxy)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



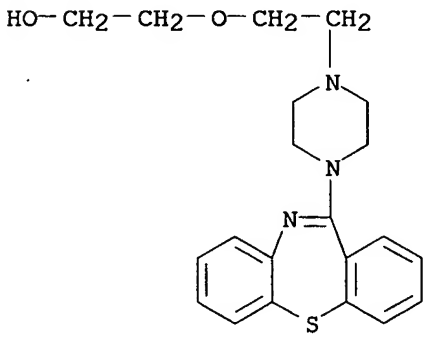
RN 753475-15-9 CAPLUS
CN Dibenzo[b,f][1,4]thiazepine, 11-(1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)



● HCl

IT **111974-69-7P**, Quetiapine **111974-72-2P**, Quetiapine hemifumarate
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of quetiapine or its salts by alkylation of piperazinyldibenzo[b,j][1,4]thiazepine hydrochloride with (chloroethoxy)ethanol in presence of phase transfer catalyst and base)

RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (9CI) (CA INDEX NAME)



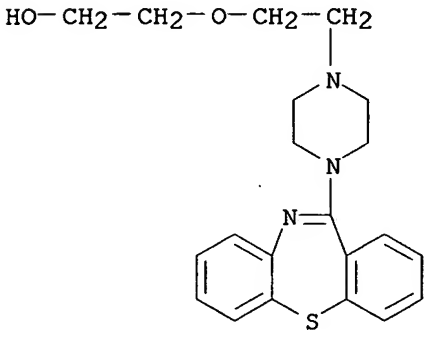
RN 111974-72-2 CAPLUS

QUETIAPINE

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

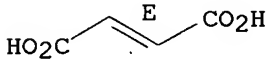
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L23 ANSWER 2 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:777597 CAPLUS
DOCUMENT NUMBER: 139:281277
TITLE: **Crystalline** forms of quetiapine hemifumarate
INVENTOR(S): Lifshitz-Liron, Revital; Kovalevski-Ishai, Eti; Dolitzky, Ben-Zion; Wizel, Shlomit; Lidor-Hadas, Rami
PATENT ASSIGNEE(S): Teva Pharmaceutical Industries Ltd., Israel; Teva Pharmaceuticals USA, Inc.
SOURCE: PCT Int. Appl., 56 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003080065	A1	20031002	WO 2003-US8898	20030320
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2479668	AA	20031002	CA 2003-2479668	20030320
US 2003216376	A1	20031120	US 2003-393929	20030320
EP 1482945	A1	20041208	EP 2003-721434	20030320
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK				

PRIORITY APPLN. INFO.:
US 2002-365913P P 20020320
US 2003-443585P P 20030129
WO 2003-US8898 W 20030320

AB The present invention relates to novel **crystalline** forms of quetiapine hemifumarate, denominated quetiapine hemifuramate form II and form III. These novel **crystalline** forms of quetiapine hemifuramate have been characterized by methods including x-ray powder diffraction (XRD), Fourier transform IR spectroscopy (FTIR), differential scanning calorimetry (DSC), and thermal gravimetric anal. (TGA). Methods for preparation of the novel **crystalline** quetiapine hemifuramate form II as chloroform solvate and dichloromethane solvate, quetiapine hemifuramate form III as chloroform solvate, and quetiapine hemifuramate form I are provided.

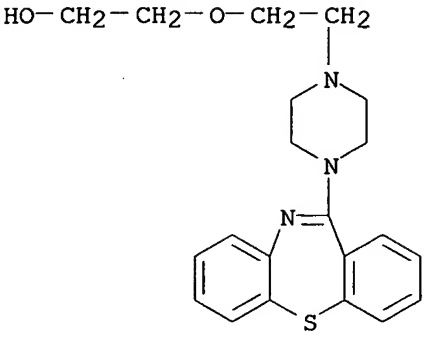
IT **111974-72-2**, Quetiapine fumarate
RL: PEP (Physical, engineering or chemical process); PRP (Properties); PYP (Physical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation and properties of **crystalline** forms of quetiapine hemifumarate)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

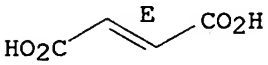
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L23 ANSWER 3 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:754995 CAPLUS
DOCUMENT NUMBER: 137:268473
TITLE: Porous drug matrices and methods of manufacture thereof
INVENTOR(S): Straub, Julie; Altreuter, David; Bernstein, Howard; Chickering, Donald E.; Khattak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere Inc., USA
SOURCE: U.S. Pat. Appl. Publ., 20 pp., Cont.-in-part of U. S. 6,395,300.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002142050	A1	20021003	US 2002-53929		20020122
US 6395300	B1	20020528	US 1999-433486		19991104
US 6645528	B1	20031111	US 2000-694407		20001023
ZA 2001010347	A	20030730	ZA 2001-10347		20011218
US 2005048116	A1	20050303	US 2004-924642		20040824
PRIORITY APPLN. INFO.:			US 1999-136323P	P	19990527
			US 1999-158659P	P	19991008
			US 1999-433486	A2	19991104
			US 2002-53929	A3	20020122

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solution and hydrophilic or hydrophobic excipients that stabilize the drug and inhibit crystallization, and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. Hydrophobic or hydrophilic excipients may be selected to stabilize the drug in **crystalline** form by inhibiting crystal growth or to stabilize the drug in amorphous form by preventing crystallization The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Thus, 5.46 g of PEG 8000, 0.545 g of prednisone, and 0.055 g of Span 40 were dissolved in 182 mL of methylene chloride. A solution of 3.27 g of ammonium bicarbonate in 18.2 mL of water was added to the organic solution (phase ratio 1:10) and homogenized for 5 min at 16,000 RPM. The resulting emulsion was spray dried on a benchtop spray dryer using an air-atomizing nozzle and nitrogen as the drying gas.

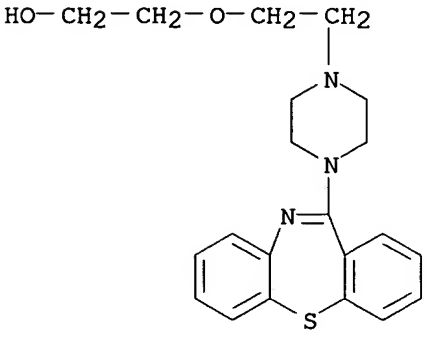
IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(porous drug matrixes and methods of manufacture thereof)

QUETIAPINE

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

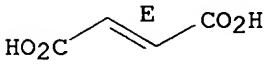
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L23 ANSWER 4 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:113658 CAPLUS
DOCUMENT NUMBER: 130:173010
TITLE: **Crystalline** dibenzothiazepine derivative and its use as an antipsychotic agent
INVENTOR(S): Snape, Evan William
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9906381	A1	19990211	WO 1998-GB2260	19980728
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2295792	AA	19990211	CA 1998-2295792	19980728
AU 9885498	A1	19990222	AU 1998-85498	19980728
AU 739255	B2	20011004		
EP 1000043	A1	20000517	EP 1998-936529	19980728
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
TR 200000848	T2	20000821	TR 2000-200000848	19980728
BR 9811061	A	20000919	BR 1998-11061	19980728
EE 200000062	A	20001016	EE 2000-200000062	19980728
JP 2001512109	T2	20010821	JP 2000-505140	19980728
NZ 501914	A	20010928	NZ 1998-501914	19980728
TW 533207	B	20030521	TW 1998-87112313	19980728
CN 1125058	B	20031022	CN 1998-807572	19980728
IL 133618	A1	20040208	IL 1998-133618	19980728
RU 2224754	C2	20040227	RU 2000-105271	19980728
ZA 9806904	A	19990201	ZA 1998-6904	19980731
MX 200000511	A	20001109	MX 2000-511	20000113
US 6372734	B1	20020416	US 2000-463452	20000127
NO 2000000484	A	20000316	NO 2000-484	20000131
HK 1029992	A1	20040709	HK 2001-100731	20010201
US 2002147186	A1	20021010	US 2002-101948	20020321
PRIORITY APPLN. INFO.:			GB 1997-16161 A	19970801
			WO 1998-GB2260 W	19980728
			US 2000-463452 A1	20000127

OTHER SOURCE(S): MARPAT 130:173010

AB **Crystalline** 11-[4-[2-(2-hydroxyethoxy) ethyl]-1-piperazinyl]-dibenzo[b,f] [1,4]thiazepine (I) may be prepared by crystallizing I from a non-aromatic solvent such as Et acetate, iso-Bu acetate, Me iso-Bu ketone or Me tert-Bu ether, preferably in the absence of water. The **cryst** . I may be converted into a pharmaceutically acceptable salt such as fumarate, to be used as an antipsychotic agent. **Crystalline** I was prepared by (1) adding water and HCl to a solution of I in toluene, (2) separating the aqueous and organic phases, (3) adding Me tert-Bu ether and a NaOH solution to the aqueous phase, (4) separating and drying the organic phase , and (5) crystallizing I

from Me tert-Bu ether.

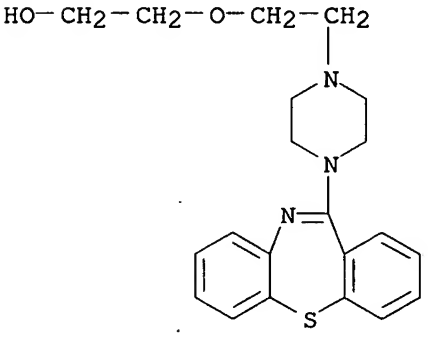
IT **111974-72-2P**
RL: IMF (Industrial manufacture); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(crystallization of antipsychotic agent [[(hydroxyethoxy)ethyl]piperazinyl]dibenzothiazepine)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

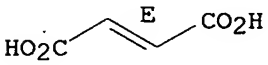
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



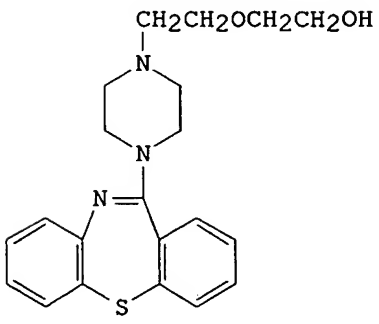
REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L23 ANSWER 5 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1989:57696 CAPLUS
DOCUMENT NUMBER: 110:57696
TITLE: Process for the preparation of a piperazinodibenzothiazepine with antidopaminergic activity
INVENTOR(S): Barker, Alan Charles; Copeland, Robert Jeffrey
PATENT ASSIGNEE(S): Imperial Chemical Industries PLC, UK
SOURCE: Eur. Pat. Appl., 8 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 282236	A1	19880914	EP 1988-301891	19880304
EP 282236	B1	19911211		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
ZA 8801350	A	19881228	ZA 1988-1350	19880225
CA 1337345	A1	19951017	CA 1988-559825	19880225
IL 85564	A1	19920525	IL 1988-85564	19880226
AU 8812378	A1	19880908	AU 1988-12378	19880229
AU 595099	B2	19900322		
DK 8801130	A	19880911	DK 1988-1130	19880302
DK 175310	B1	20040816		
AT 70271	E	19911215	AT 1988-301891	19880304
ES 2037822	T3	19930701	ES 1988-301891	19880304
HU 50336	A2	19900129	HU 1988-1086	19880307
HU 202231	B	19910228		
DD 271703	A5	19890913	DD 1988-313500	19880308
FI 8801087	A	19880911	FI 1988-1087	19880309
FI 87778	B	19921113		
FI 87778	C	19930225		
NO 8801044	A	19880912	NO 1988-1044	19880309
NO 174421	B	19940124		
NO 174421	C	19940504		
JP 63243081	A2	19881007	JP 1988-55092	19880310
JP 06088991	B4	19941109		

PRIORITY APPLN. INFO.: GB 1987-5574 A 19870310
EP 1988-301891 A 19880304
OTHER SOURCE(S): MARPAT 110:57696
GI



I

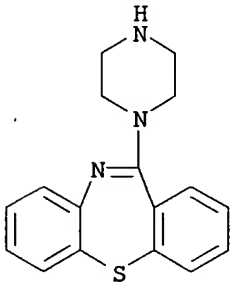
QUETIAPINE

AB A process for preparing the title compound I or a salt thereof, which has antidopaminergic activity and may be used, e.g., as an antipsychotic agent or as a treatment for hyperactivity (no data), comprised reacting 11-piperazinodibenzo[b,f]-1,4-thiazepine (II) with XCH2CH2OCH2CH2OH (III; X = atom or group removable as an anion) and, when I is obtained as a base and a salt is required, reacting said I with an acid to afford a salt and when I is obtained as a salt and a base is required, treating said I with a base. 2-H2NC6H4SPh reacted with ClCO2Ph to give .apprx.90% 2-PhSC6H4NHCO2Ph which was cyclized with polyphosphoric acid to give .apprx.87% dibenzo[b,f]-1,4-thiazepin-11(10H)-one. Treating this with POCl3 and PhNMe2 gave 92.6% 11-chlorodibenzo[b,f]-1,4-thiazepine which condensed with piperazine to give .apprx.88% II isolated as the di-HCl salt. Alkylation with III (X = Cl) in refluxing PrOH and N-methylpyrrolidone containing Na2CO3 and NaI 24 h gave 78% I isolated as the hemi-fumarate.

IT **5747-48-8P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and reaction of, in synthesis of antidopaminergic agent)

RN 5747-48-8 CAPLUS

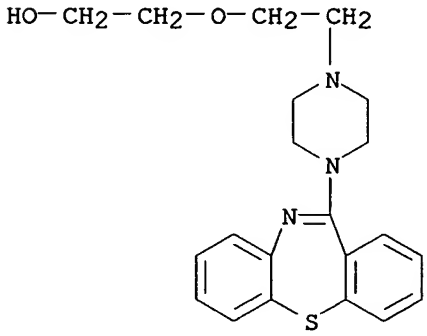
CN Dibenzo[b,f][1,4]thiazepine, 11-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA INDEX NAME)



IT **111974-69-7P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of as antidopaminergic agent)

RN 111974-69-7 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (9CI) (CA INDEX NAME)



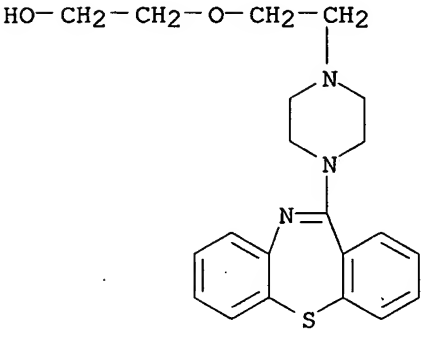
IT **111974-72-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)

QUETIAPINE

(preparation of, as antidopaminergic agent)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

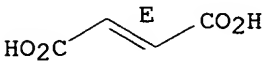
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



IT **628-89-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of, in synthesis of antidopaminergic dibenzothiazepine derivative)
RN 628-89-7 CAPLUS
CN Ethanol, 2-(2-chloroethoxy)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

QUETIAPINE

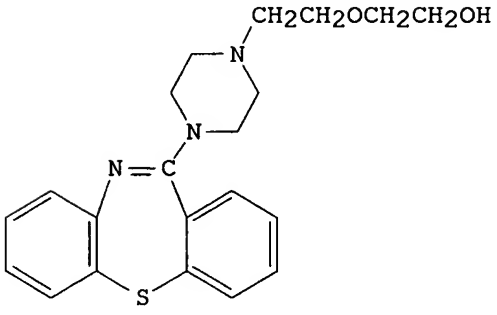
L23 ANSWER 6 OF 6 CAPLUS COPYRIGHT 2005 ACS on STN

ACCESSION NUMBER:	1988:37876 CAPLUS
DOCUMENT NUMBER:	108:37876
TITLE:	Preparation of 11-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]dibenzo[b,f][1,4]thiazepine as a neuroleptic and antipsychotic
INVENTOR(S):	Warawa, Edward John; Migler, Bernard Martin
PATENT ASSIGNEE(S):	ICI Americas, Inc., USA
SOURCE:	Eur. Pat. Appl., 18 pp. CODEN: EPXXDW
DOCUMENT TYPE:	Patent
LANGUAGE:	English
FAMILY ACC. NUM. COUNT:	1
PATENT INFORMATION:	

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 240228	A1	19871007	EP 1987-302539	19870324
EP 240228	B1	19901107		
R: AT, BE, CH, DE, ES, FR, GB, GR, IT, LI, LU, NL, SE				
FI 8701137	A	19870928	FI 1987-1137	19870316
FI 86059	B	19920331		
FI 86059	C	19920710		
ZA 8701940	A	19871125	ZA 1987-1940	19870317
DD 259403	A5	19880824	DD 1987-300862	19870317
IL 81923	A1	19910310	IL 1987-81923	19870318
AU 8770459	A1	19871001	AU 1987-70459	19870320
AU 593336	B2	19900208		
US 4879288	A	19891107	US 1987-28473	19870320
AT 58132	E	19901115	AT 1987-302539	19870324
NO 8701267	A	19870928	NO 1987-1267	19870326
NO 168771	B	19911223		
NO 168771	C	19920401		
DK 8701585	A	19870928	DK 1987-1585	19870327
DK 174618	B1	20030721		
JP 63008378	A2	19880114	JP 1987-71962	19870327
JP 06004606	B4	19940119		
HU 47568	A2	19890328	HU 1987-1342	19870327
HU 201062	B	19900928		
CA 1288428	A1	19910903	CA 1987-533171	19870327

PRIORITY APPLN. INFO.:	GB 1986-7684	A	19860327
	EP 1987-302539	A	19870324

GI



I

QUETIAPINE

AB The title compound (I) and its salts, useful as antipsychotics and neuroleptics, were prepared by amination of the corresponding imino chloride or thioether with 1-[2-(2-hydroxyethoxy)ethyl]piperazine (II). Dibenzo[b,f][1,4]thiazepine-11(10H)-one, POCl3, and PhNMe2 were heated 6 h to give the intermediate imino chloride, which was refluxed with II in xylene for 30 h to give 77.7% I. I.HCl at 80 mg/kg i.p. eliminated apomorphine-induced climbing in mice. Tablets were prepared containing I 5, lactose 88, Mg stearate 1, polyvinylpyrrolidone 2, and Na starch glycolate 4 mg.

IT **628-89-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(alkylation by, of piperazinyldibenzothiazepine derivative)

RN 628-89-7 CAPLUS

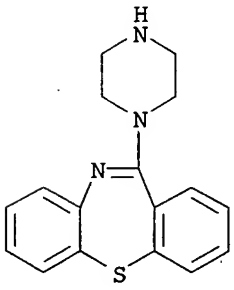
CN Ethanol, 2-(2-chloroethoxy)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)

$ClCH_2-CH_2-O-CH_2-CH_2-OH$

IT **111974-74-4P**
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation and alkylation of, by chloroethoxyethanol)

RN 111974-74-4 CAPLUS

CN Dibenzo[b,f][1,4]thiazepine, 11-(1-piperazinyl)-, dihydrochloride (9CI) (CA INDEX NAME)



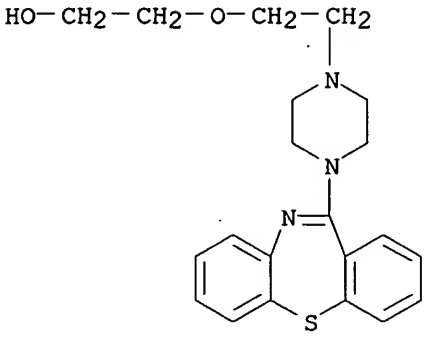
●2 HCl

IT **111974-69-7P 111974-71-1P 111974-72-2P**
111997-26-3P
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of, as antipsychotic and neuroleptic)

RN 111974-69-7 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]- (9CI) (CA INDEX NAME)

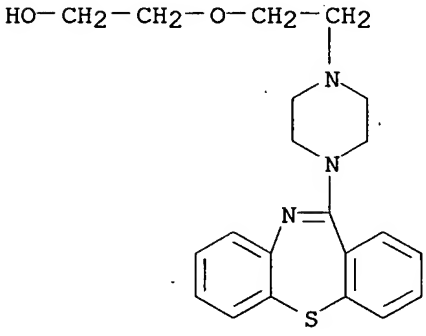
QUETIAPINE



RN 111974-71-1 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2Z)-2-butenedioate (1:1) (salt) (9CI) (CA INDEX NAME)

CM 1

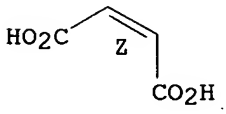
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-16-7
CMF C4 H4 O4

Double bond geometry as shown.

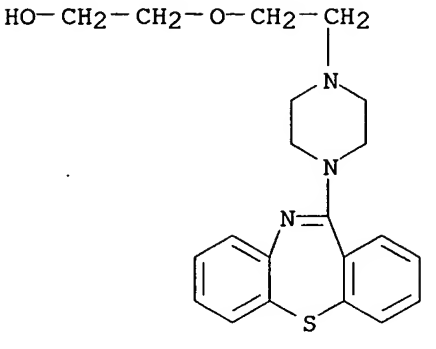


RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

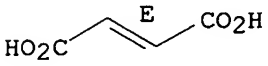
QUETIAPINE



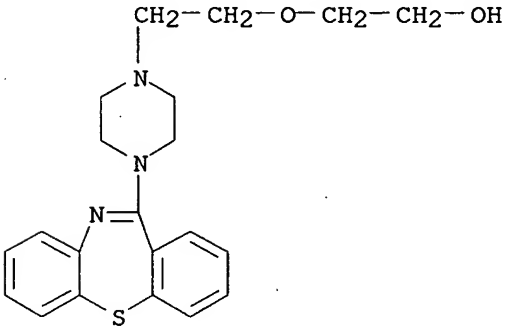
CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



RN 111997-26-3 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, dihydrochloride (9CI) (CA INDEX NAME)



●2 HCl

QUETIAPINE

=> => => d ibib abs hitstr 1-98

QUETIAPINE

L26 ANSWER 1 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2005:120908 CAPLUS
DOCUMENT NUMBER: 142:198109
TITLE: Process for the preparation of 11-(1-piperazinyl)dibenzo[b,f][1,4]thiazepine an intermediate in the synthesis of the antipsychotic drug quetiapine
INVENTOR(S): Kaczmarek, Lukasz; Badowska-Roslonek, Katarzyna; Stolarczyk, Elzbieta; Szelejewski, Wieslaw
PATENT ASSIGNEE(S): Helm AG, Germany; Instytut Farmaceutyczny
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2005012274	A1	20050210	WO 2004-EP51520	20040716

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

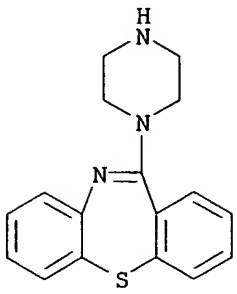
PRIORITY APPLN. INFO.: PL 2003-361347 A 20030718

AB A process for the preparation of 11-(1-piperazinyl)dibenzo[b,f][1,4]thiazepine (I) comprising reacting Ph 2-(phenylthio) phenylcarbamate with piperazine and cyclizing the obtained N-[(2-phenylthio)phenyl]-1-piperazinylcarboxamide in a presence of cyclizing agent. I is an intermediate in the synthesis of the antipsychotic drug quetiapine.

IT **753475-15-9P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(in a process for the preparation of 11-(1-piperazinyl)dibenzo[b,f][1,4]thiazepine an intermediate in the synthesis of the antipsychotic drug quetiapine)

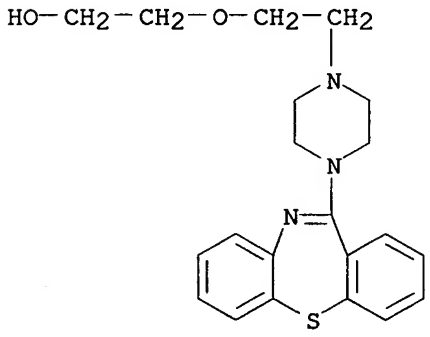
RN 753475-15-9 CAPLUS
CN Dibenzo[b,f][1,4]thiazepine, 11-(1-piperazinyl)-, monohydrochloride (9CI) (CA INDEX NAME)

QUETIAPINE

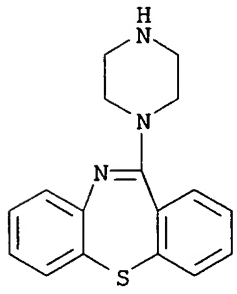


● HCl

IT **111974-69-7P**, Quetiapine
RL: PNU (Preparation, unclassified); PREP (Preparation)
(preparation of)
RN 111974-69-7 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-
(9CI) (CA INDEX NAME)

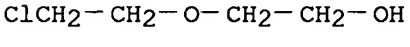


IT **5747-48-8P**, 11-(1-Piperazinyl)dibenzo[b,f][1,4]thiazepine
RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT
(Reactant or reagent)
(process for the preparation of 11-(1-piperazinyl)dibenzo[b,f][1,4]thiazepin
e an intermediate in the synthesis of the antipsychotic drug
quetiapine)
RN 5747-48-8 CAPLUS
CN Dibenzo[b,f][1,4]thiazepine, 11-(1-piperazinyl)- (7CI, 8CI, 9CI) (CA
INDEX NAME)



QUETIAPINE

IT **628-89-7**
RL: RCT (Reactant); RACT (Reactant or reagent)
(reaction of)
RN 628-89-7 CAPLUS
CN Ethanol, 2-(2-chloroethoxy)- (6CI, 7CI, 8CI, 9CI) (CA INDEX NAME)



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 2 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:892420 CAPLUS
DOCUMENT NUMBER: 141:360592
TITLE: The atypical antipsychotic quetiapine increases both noradrenaline and dopamine release in the rat prefrontal cortex
AUTHOR(S): Pira, Luigi; Mongeau, Raymond; Pani, Luca
CORPORATE SOURCE: Neuroscienze PharmaNess SCaRL, Cagliari, 09124, Italy
SOURCE: European Journal of Pharmacology (2004), 504(1-2), 61-64
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

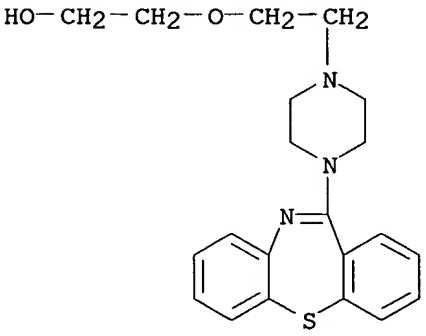
AB Quetiapine is a novel atypical antipsychotic drug with multi-receptor affinity. Using in vivo microdialysis, we investigated if quetiapine modulates extracellular noradrenaline and dopamine in brain areas generally believed to be involved in the pathophysiol. of schizophrenia and in the action of antipsychotic drugs. Quetiapine (5, 10 and 20 mg/kg, i.p.) increased levels of noradrenaline in both the prefrontal cortex and the caudate nucleus, while it increased dopamine levels mainly in the prefrontal cortex. It is argued that the marked increase of dopaminergic transmission in the prefrontal cortex induced by quetiapine might be relevant to its therapeutical action.

IT **111974-72-2**, Quetiapine fumarate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotic quetiapine increases both noradrenaline and dopamine release in rat prefrontal cortex)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

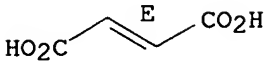


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



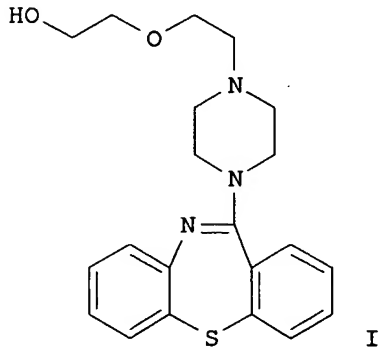
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 3 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:756700 CAPLUS
DOCUMENT NUMBER: 141:265936
TITLE: Novel polymorphs of quetiapine fumarate
INVENTOR(S): Parthasaradhi, Reddy Bandi; Rathnakar, Reddy Kura; Raji, Reddy Rapolu; Muralidhara, Reddy Dasari; Subash Chander, Reddy Kesireddy
PATENT ASSIGNEE(S): Hetero Drugs Limited, India
SOURCE: PCT Int. Appl., 17 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004078735	A1	20040916	WO 2003-IN43	20030303
WO 2004078735	C2	20041223		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 2004242562	A1	20041202	US 2004-488628	20040303
PRIORITY APPLN. INFO.:			WO 2003-IN43 W	20030303

GI



I

AB The present invention relates to novel polymorphic forms of quetiapine (I) fumarate, processes for their preparation and pharmaceutical compns. containing them. I fumarate was prepared from the base and fumaric acid in acetone and Et acetates to give a form I.

IT **111974-72-2P**, Quetiapine fumarate
RL: PRP (Properties); SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
(polymorphs of quetiapine fumarate)

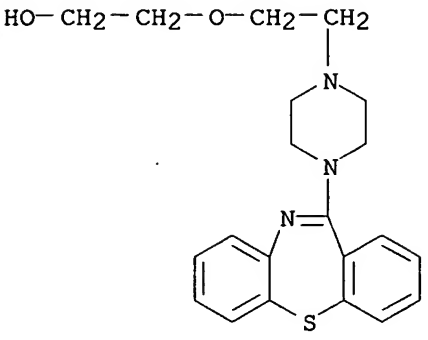
RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

QUETIAPINE

CM 1

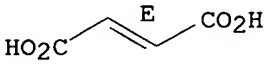
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 4 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:751460 CAPLUS
DOCUMENT NUMBER: 142:126538
TITLE: PREDICT modeling and in-silico screening for G-protein coupled receptors
AUTHOR(S): Shacham, Sharon; Marantz, Yael; Bar-Haim, Shay; Kalid, Ori; Warshaviak, Dora; Avisar, Noa; Inbal, Boaz; Heifetz, Alexander; Fichman, Merav; Topf, Maya; Naor, Zvi; Noiman, Silvia; Becker, Oren M.
CORPORATE SOURCE: Predix Pharmaceuticals Ltd, Ramat Gan, Israel
SOURCE: Proteins: Structure, Function, and Bioinformatics (2004), 57(1), 51-86
CODEN: PSFBAF
PUBLISHER: Wiley-Liss, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB G-protein coupled receptors (GPCRs) are a major group of drug targets for which only one x-ray structure is known (the nondrugable rhodopsin), limiting the application of structure-based drug discovery to GPCRs. In this paper the authors present the details of PREDICT, a new algorithmic approach for modeling the 3D structure of GPCRs without relying on homol. to rhodopsin. PREDICT, which focuses on the transmembrane domain of GPCRs, starts from the primary sequence of the receptor, simultaneously optimizing multiple 'decoy' conformations of the protein in order to find its most stable structure, culminating in a virtual receptor-ligand complex. In this paper the authors present a comprehensive anal. of three PREDICT models for the dopamine D2, neurokinin NK1, and neuropeptide Y Y1 receptors. A shorter discussion of the CCR3 receptor model is also included. All models were found to be in good agreement with a large body of exptl. data. The quality of the PREDICT models, at least for drug discovery purposes, was evaluated by their successful utilization in in-silico screening. Virtual screening using all three PREDICT models yielded enrichment factors 9-fold to 44-fold better than random screening. Namely, the PREDICT models can be used to identify active small-mol. ligands embedded in large compound libraries with an efficiency comparable to that obtained using crystal structures for non-GPCR targets.

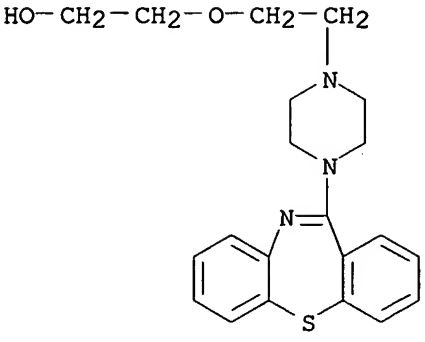
IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); PRP (Properties); BIOL (Biological study)
(PREDICT modeling and in-silico screening for G-protein coupled receptors)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

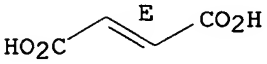
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 187 THERE ARE 187 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 5 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:688762 CAPLUS
DOCUMENT NUMBER: 141:271401
TITLE: Quetiapine in schizophrenia: onset of action within the first week of treatment
AUTHOR(S): Small, Joyce G.; Kolar, Madeleine C.; Kellams, Jeffrey J.
CORPORATE SOURCE: Larue D. Carter Memorial Hospital, Indiana University School of Medicine, Indianapolis, USA
SOURCE: Current Medical Research and Opinion (2004), 20(7), 1017-1023
CODEN: CMROCX; ISSN: 0300-7995
PUBLISHER: LibraPharm Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

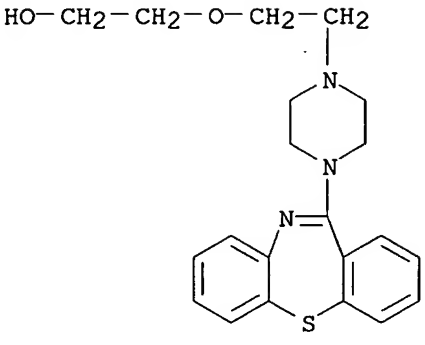
AB Objective: Three placebo-controlled clin. trials have established the efficacy of the atypical antipsychotic quetiapine (Seroquel*) in schizophrenia. These trials were designed and powered to detect a treatment difference in the primary endpoint at Week 6. The objective of the current anal. was to investigate the effect of quetiapine at earlier time-points. Research design and methods: A combined anal. of data from three acute, double-blind, placebo-controlled, randomized trials was carried out. The trials comprised hospitalized patients with an acute exacerbation of chronic or subchronic schizophrenia who were randomized to receive quetiapine 150-750 mg/day (n = 422) or placebo (n=198). Symptoms were assessed using changes from baseline to Week 1 in the Brief Psychiatric Rating Scale (BPRS) total score, BPRS pos. symptom cluster score and the individual BPRS items of excitement, tension and depression. Changes from baseline to Weeks 1-6 were calculated for BPRS Factor I scores (which measures mood symptoms) and Scale for Assessment of Neg. Symptoms (SANS) summary scores. Results: Within 1 wk, overall symptom improvement (BPRS total score) was significantly ($p < 0.05$) greater with quetiapine than with placebo; improvement also occurred in individual BPRS items of excitement, tension and depression. Improvement in neg. symptoms was significantly ($p < 0.05$) greater with quetiapine than with placebo from Week 1, as was the BPRS Factor I score from Week 2. More quetiapine- than placebo-treated patients showed a response of pos. symptoms to treatment within 1 wk ($p < 0.05$). The beneficial effects of quetiapine are observed within 1 wk across a broad spectrum of symptoms.

IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(Quetiapine; quetiapine therapy for schizophrenia)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

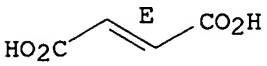
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 6 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:633461 CAPLUS
DOCUMENT NUMBER: 141:167815
TITLE: Use of N-desmethylclozapine to treat human neuropsychiatric disease
INVENTOR(S): Weiner, David M.; Brann, Mark R.
PATENT ASSIGNEE(S): Acadia Pharmaceuticals Inc, USA
SOURCE: PCT Int. Appl., 27 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2004064753	A2	20040805	WO 2004-US1509	20040121
WO 2004064753	A3	20041125		
W: AE, AE, AG, AL, AL, AM, AM, AM, AT, AT, AU, AZ, AZ, BA, BB, BG, BG, BR, BR, BW, BY, BY, BZ, BZ, CA, CH, CN, CN, CO, CO, CR, CR, CU, CU, CZ, CZ, DE, DE, DK, DK, DM, DZ, EC, EC, EE, EE, EG, ES, ES, FI, FI, GB, GD, GE, GE, GH, GM, HR, HR, HU, HU, ID, IL, IN, IS, JP, JP, KE, KE, KG, KG, KP, KP, KP, KR, KR, KZ, KZ, KZ, LC, LK, LR, LS, LS, LT, LU, LV, MA, MD, MD, MG, MK, MN, MW, MX, MX, MZ, MZ, NA, NI				
US 2004224942	A1	20041111	US 2004-761787	20040121
PRIORITY APPLN. INFO.:			US 2003-442690P P	20030123

AB Disclosed herein is a method to treat neuropsychiatric diseases including psychosis, affective disorders, dementia, neuropathic pain, and glaucoma. Treatment is carried out by administering a therapeutically effective amount of N-desmethylclozapine to a patient suffering from a neuropsychiatric disease.

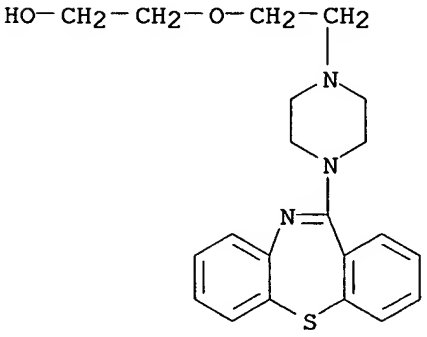
IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(desmethylclozapine to treat human neuropsychiatric disease)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

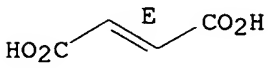


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 7 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:630525 CAPLUS
DOCUMENT NUMBER: 141:235429
TITLE: Pharmacological treatment strategies for schizophrenia
AUTHOR(S): Lindenmayer, J. P.; Khan, Anzalee
CORPORATE SOURCE: Psychopharmacology Research Unit, Manhattan Psychiatric Center, Wards Island, NY, 10035, USA
SOURCE: Expert Review of Neurotherapeutics (2004), 4(4), 705-723
CODEN: ERNXAR; ISSN: 1473-7175
PUBLISHER: Future Drugs Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

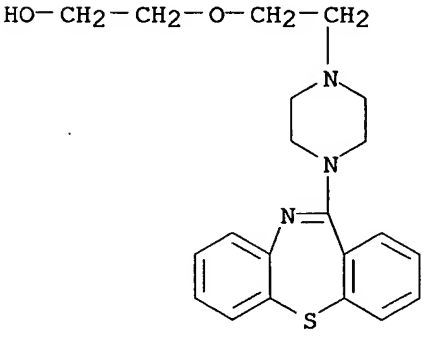
AB A review. The pharmacol. choices for the treatment of schizophrenia have been greatly expanded with the availability of the atypical compds. clozapine (Clozaril, Novartis), risperidone (Risperdal, Janssen-Cilag), olanzapine (Zyprexa, Ell Lilly & Co.), quetiapine (Seroquel, AstraZeneca), ziprasidone (Geodon, Pfizer inc.) and aripiprazole (Abilify, Otsuka Pharmaceutical Co. Ltd). In this article, the effects of the newer antipsychotics and their side effects are reviewed. Key issues in acute and maintenance treatment, often lifelong, will be reviewed. Side-effect management to ensure adherence to an optimal treatment regimen will be discussed. Coexisting syndromes must be treated in concordance with the patient's clin. presentation. For treatment-resistant patients, atypical compds. are generally more effective than their typical counterparts but medication augmentation strategies are frequently recommended. Finally, the results of recent meta-analyses comparing the effects of atypical vs. typical compds. will be critically reviewed and remaining gaps in the current pharmacotherapy of schizophrenia will be explored.

IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmacol. treatment strategies for schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



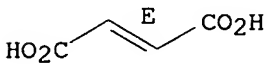
CM 2

CRN 110-17-8

QUETIAPINE

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 100 THERE ARE 100 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

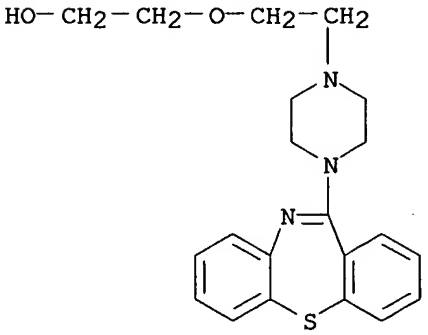
L26 ANSWER 8 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:480279 CAPLUS
DOCUMENT NUMBER: 142:147760
TITLE: Determination of quetiapine fumarate in serum by HPLC with ultraviolet detection
AUTHOR(S): Li, Wenbiao; Xue, Yazhen; Zhai, Yimin; Zhang, Jun; Guo, Guixin; Wang, Chuanyue; Cai, Zhuoji
CORPORATE SOURCE: Laboratory of Clinical Psychopharmacology, Beijing Anding Hospital, Capital University Medical Sciences, Beijing, 100088, Peop. Rep. China
SOURCE: Yaowu Fenxi Zazhi (2003), 23(4), 247-251
CODEN: YFZADL; ISSN: 0254-1793
PUBLISHER: Yaowu Fenxi Zazhi Bianji Weiyuanhui
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

AB A method for the determination of quetiapine fumarate in serum was developed using HPLC on Inertsil ODS-3 C18 reversed column (5 μm, 4.6 mm x 150 mm) with the UV detection wavelength of 254 nm. The mobile phase consisted of methanol-acetonitrile-water (17.6 : 36.8 : 45.6, added by 0.8 mL glacial acetic acid and 1.2 mL n- butanol in 100 mL) and loxapine succinate salt was used as the internal standard 1 ML Sample serum was extracted with 4 mL distilled di-Et ether and re-extracted with 0.1 mol L-1 HCl, 0.2 mL. The HCl phase was evaporated to dry with N2 stream at 80- 100° and the residues were dissolved with 50 μL mobile phase. The relationship of the peak height ratio of quetiapine to loxapine vs quetiapine fumarate concentration in serum was linear within the range of 3.125 - 3200 μg L-1 with r 0.9997. The lowest detection limit was 0.64 ng and the lowest concentration detected was 2 μg L-1. The extraction recovery of quetiapine fumarate and loxapine succinate salt was 80.38% - 83.87% with RSD 4.2% - 7.6%, the intra- and inter-day was 3.3% - 5.8 and 2.7% - 8.0%, resp. The method was sensitive, precise, reproducible and specific and could be used in the pharmacokinetic research and therapeutic monitoring of quetiapine fumarate.

IT **111974-72-2**, Quetiapine fumarate
RL: PKT (Pharmacokinetics); BIOL (Biological study)
(determination of quetiapine fumarate in serum by HPLC with UV detection)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

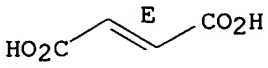


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 9 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:304280 CAPLUS
DOCUMENT NUMBER: 141:374305
TITLE: Combination of bupropion, paroxetine and quetiapine as adjuvant treatment for multiple myeloma
AUTHOR(S): Kast, Richard E.; Lewin Altschuler, Eric
CORPORATE SOURCE: College of Medicine, Department of Psychiatry, University of Vermont, Burlington, VT, 04501, USA
SOURCE: Medical Hypotheses (2004), 62(5), 817-818
CODEN: MEHYDY; ISSN: 0306-9877
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

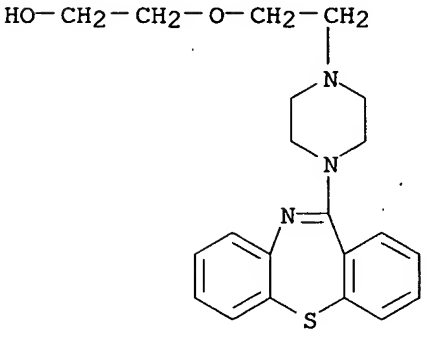
AB A review. Multiple myeloma is a severe plasma dyschrasia with no known treatment or cure, even bone marrow transplantation. Cytokines such as tumor necrosis factor-α (TNF) and interleukin-6 (Il-6) are thought to be important trophic factors for the malignant plasma cells. In turn, histamine and nitric oxide are pos. regulatory factors for Il-6. Here we note that the safe, approved and commonly used psychiatric medicines bupropion (Wellbutrin), paroxetine (Paxil) and quetiapine (Seroquel) are resp. potent TNF, nitric oxide and histamine antagonists and thus might find some use in treatment of multiple myeloma.

IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(bupropion, paroxetine, seroquel (quetiapine) are safe and potent TNF, NO, histamine antagonist and should be considered for use alone or in combination for multiple myeloma adjuvant treatment)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

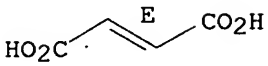


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



REFERENCE COUNT: 12 THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 10 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2004:113842 CAPLUS
DOCUMENT NUMBER: 141:64302
TITLE: Determination of quetiapine fumarate level in serum by HPLC
AUTHOR(S): Zhang, Shining; Li, Yi; Yao, Hui
CORPORATE SOURCE: Institute of Nanjing Brain Hospital, Nanjing Medical University, Nanjing, 210029, Peop. Rep. China
SOURCE: Zhongguo Yiyuan Yaoxue Zazhi (2002), 22(11), 673-675
CODEN: ZYYAEP; ISSN: 1001-5213
PUBLISHER: Zhongguo Yiyuan Yaoxue Zazhi Bianjibu
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

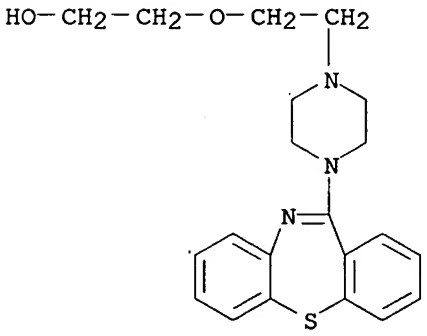
AB A HPLC method for the determination of quetiapine fumarate level in human serum was established by using HPLC on C18 column with methanol:water:1 mol L-1 ammonium acetate:5 mol L-1 NH4OH. The quetiapine fumarate level was determined by means of external standard method. The linearity was obtained from 10-300 μg L-1 of quetiapine fumarate level in serum with a good correlation (r = 0.9997). Detection limit was 5 μg L-1. The average extraction recovery was 93.10% with intra- and inter-day RSD 3.41% and 4.16%, resp. HPLC could be used for the detection of quetiapine fumarate in human serum.

IT **111974-72-2**, Quetiapine fumarate
RL: ANT (Analyte); ANST (Analytical study)
(determination of quetiapine fumarate level in serum by HPLC)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

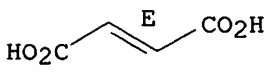
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

QUETIAPINE

L26 ANSWER 11 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:829447 CAPLUS
DOCUMENT NUMBER: 140:209812
TITLE: Determination of quetiapine fumarate in blood plasma
AUTHOR(S): Wen, Yumei; Chen, Weijia; Lu, Runji; Lu, Xinqiao
CORPORATE SOURCE: Lab. of Clinical Pharmacology, Guangzhou Brain Hospital, Guangzhou, 510370, Peop. Rep. China
SOURCE: Zhongguo Linchuang Yaoxue Zazhi (2003), 12(4), 215-217
CODEN: ZLYZA5; ISSN: 1007-4406
PUBLISHER: Zhongguo Linchuang Yaoxue Zazhishe
DOCUMENT TYPE: Journal
LANGUAGE: Chinese

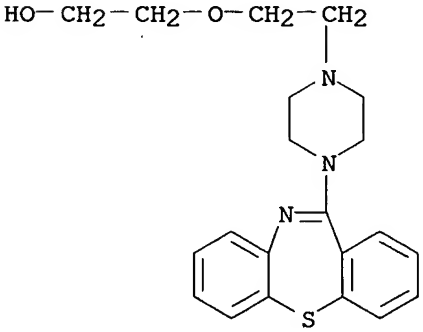
AB The objective of this study was to develop an HPLC method for quant. determination of quetiapine fumarate (QTP) in blood plasma. QTP was extracted with Et acetate. The residue dissolved was analyzed with a reverse phase HPLC system (C18 column, 250 mm + 4.6 mm, 5 μm); mobile phase: MeOH-H2O (85:15, volume/volume); UV detection: 254 nm. The average recoveries for QTP were 98.20%, 101.44% and 98.21% for 3 concns., resp. The within-day and between-day RSD was lower than 5% (n = 5). The calibration curves for QTP had good linearity, r = 0.9999 (n = 11) within a concentration range of 0.17-100.00 μg mL-1. The limits of quantitation for QTP were 0.08 μg mL-1 (rsN = 2). Thus, the method provides a sensitive, accurate, precise and reliable anal. procedure for clin. monitoring of QTP in blood plasma and pharmacokinetic studies.

IT **111974-72-2**, Quetiapine fumarate
RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
(therapeutic drug monitoring; determination of quetiapine fumarate in blood plasma)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

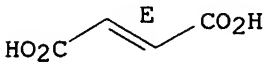


CM 2

CRN 110-17-8
CMF C4 H4 O4

QUETIAPINE

Double bond geometry as shown.



QUETIAPINE

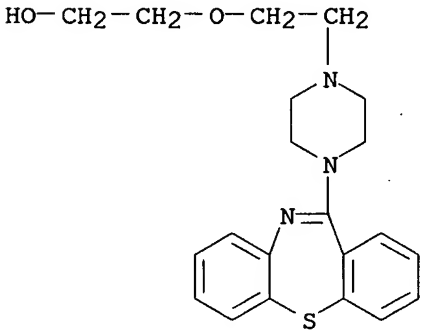
L26 ANSWER 12 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:780165 CAPLUS
DOCUMENT NUMBER: 140:246756
TITLE: Atypical antipsychotic drugs and glucose dysregulation
AUTHOR(S): Lee, Sun-Woo
CORPORATE SOURCE: Department of Psychiatry, College of Medicine, Chungnam National University, S. Korea
SOURCE: Chungnam Uidae Chapchi (2002), 29(2), 91-97
CODEN: CUCHDS; ISSN: 0253-6307
PUBLISHER: Chungnam National University, College of Medicine
DOCUMENT TYPE: Journal
LANGUAGE: Korean

AB Glucose dysregulation in patients who are medicated with atypical antipsychotics, was evaluated. Thirty one subjects were enrolled by random selection. Subjects had a psychiatric interview, including completion of various socio-demog. variables and a disease-related variable. Blood glucose levels, HbA1c level, and liver enzyme series (AST, ALT etc) were assessed. In 3 of 28 cases, new-onset, marked glucose intolerance developed and 3 of the 28 had impaired fasting glycemia after treatment with atypical antipsychotics. There were significant differences in liver enzyme (AST, ALT) levels and the total cholesterol level between the normal subjects group and the glucose dysregulation group. Atypical antipsychotics may be associated with new-onset glucose intolerance. Therefore, monitoring for changes in blood glucose levels in patients taking atypical antipsychotics may be indicated. More systematic study data are clearly needed.

IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(atypical antipsychotic drug effects on blood glucose levels)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

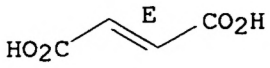


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



/QUETIAPINE

L26 ANSWER 13 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:598290 CAPLUS
DOCUMENT NUMBER: 139:386545
TITLE: Quality control of commercial tablets containing the novel antipsychotic quetiapine
AUTHOR(S): Pucci, Vincenzo; Mandrioli, Roberto; Ferranti, Anna; Furlanetto, Sandra; Augusta Raggi, Maria
CORPORATE SOURCE: Department of Pharmaceutical Sciences, University of Bologna, Bologna, 40126, Italy
SOURCE: Journal of Pharmaceutical and Biomedical Analysis (2003), 32(4-5), 1037-1044
CODEN: JPBADA; ISSN: 0731-7085
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

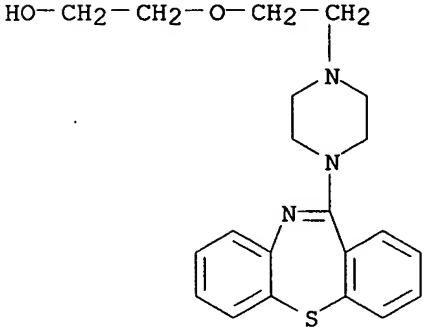
AB Quetiapine (bis [2-(2-[4-(dibenzo[b,f][1,4]thiazepin-11-yl)]ethoxy)ethanol]fumarate) is the most recent agent introduced on the drug market for the treatment of psychotic disorders. Two different anal. methods for the quality control of quetiapine in com. formulations have been developed and compared: a spectrophotometric method and a capillary zone electrophoretic (CZE) method. The spectrophotometric assay was carried out measuring the absorbance at a wavelength of 246 nm. The CZE method used an uncoated fused-silica capillary and a pH 2.5, 50 mM phosphate buffer as the background electrolyte. The detection wavelength was 205 nm, the separation voltage was 15 kV, and a complete electrophoretic run lasts less than 2.5 min. Extraction of quetiapine from the com. tablets consisted of a simple one-step treatment with a pH 2.5, 50 mM phosphate buffer. Linearity was observed in the 5-25 μg ml-1 concentration range of quetiapine for the spectrophotometric method, and in the 5-50 μg ml-1 concentration range for the electrophoretic method. Both methods gave satisfactory results in terms of repeatability and intermediate precision (RSD<1.9%). Also accuracy values were very good for both methods, the recovery being between 98.2 and 100.5%.

IT **111974-72-2**, Quetiapine fumarate
RL: ANT (Analyte); ANST (Analytical study)
(determination of antipsychotic quetiapine in com. tablets by spectroscopy and capillary zone electrophoresis)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

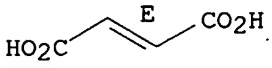


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 14 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:573981 CAPLUS
DOCUMENT NUMBER: 139:207666
TITLE: Differential effect of quetiapine on depressive symptoms in patients with partially responsive schizophrenia
AUTHOR(S): Emsley, Robin A.; Buckley, Peter; Jones, A. Martin; Greenwood, Michael R.
CORPORATE SOURCE: Department of Psychiatry, University of Stellenbosch, Cape Town, S. Afr.
SOURCE: Journal of Psychopharmacology (London, United Kingdom) (2003), 17(2), 210-215
CODEN: JOPSEQ; ISSN: 0269-8811
PUBLISHER: Sage Publications Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB While atypical antipsychotics appear to be effective in reducing depressive symptoms in the acute phase of schizophrenia, little is known about their efficacy in patients with ongoing symptoms. The present study assessed whether quetiapine (Seroquel) is more effective than haloperidol in treating depressive symptoms in patients with persistent pos. symptoms, and investigated whether this effect is independent, or secondary to, redns. in other symptoms such as pos., neg. or extrapyramidal symptoms. Patients with schizophrenia and a history of partial refractoriness to conventional antipsychotics who had not responded to 4 wk of fluphenazine treatment (20 mg/day) were randomized to receive either quetiapine (600 mg/day) or haloperidol (20 mg/day) for a further 8 wk. Change in the Pos. and Neg. Syndrome Scale depression factor score from baseline to endpoint was calculated and path analyses were performed on data from 269 patients. Quetiapine produced a greater reduction in depressive scores than haloperidol (-1.60 vs. -0.54; p = 0.006). The path analyses indicated that this was a direct effect on depressive symptoms. These findings extend the evidence for an antidepressant effect for the novel antipsychotics in schizophrenia, and suggest that this is not limited to acutely psychotic patients.

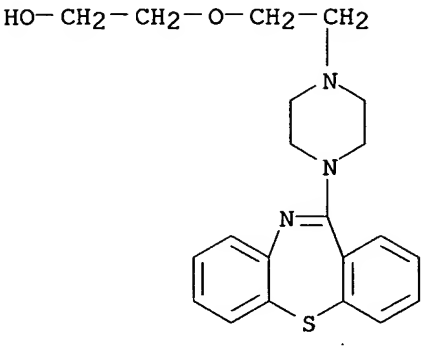
IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential effect of quetiapine on depressive symptoms in patients with partially responsive schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

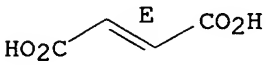
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 45 THERE ARE 45 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 15 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:532347 CAPLUS
DOCUMENT NUMBER: 139:79173
TITLE: Methods and compositions using a cyclooxygenase 2 (COX-2) inhibitor for the treatment of psychiatric disorders
INVENTOR(S): Muller, Norbert
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 27 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2003130334	A1	20030710	US 2002-157969		20020531
PRIORITY APPLN. INFO.:			DE 2001-10129328	A	20010619
			US 2002-364904P	P	20020314

OTHER SOURCE(S): MARPAT 139:79173

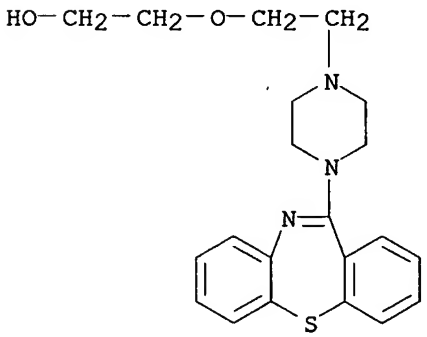
AB A method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia, is described which comprises administering a COX-2 inhibitor, or prodrug thereof, to a subject. Moreover, a method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia or a depressive disorder, is disclosed, comprising administering to a subject a COX-2 inhibitor or prodrug thereof in combination with a neuroleptic drug or an antidepressant. Compns. and kits that are suitable for the practice of the method are also described.

IT **111974-72-2**, Quetiapine fumarate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitor for treatment of psychiatric disorders, and use with other agents)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

QUETIAPINE

CRN 110-17-8
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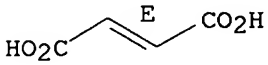


QUETIAPINE

L26 ANSWER 16 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:516070 CAPLUS
DOCUMENT NUMBER: 140:35112
TITLE: Improvement without impairment: A review of clinical data for quetiapine in the treatment of schizophrenia
AUTHOR(S): Tandon, Rajiv
CORPORATE SOURCE: University of Michigan Medical Center, Ann Arbor, MI, 48109, USA
SOURCE: Journal of Clinical Psychopharmacology (2003), 23(3, Suppl. 1), S15-S20
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

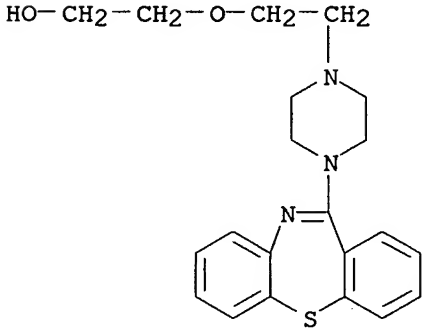
AB A review. Quetiapine fumarate is an atypical antipsychotic medication approved for the treatment of patients with schizophrenia and other psychotic disorders. Quetiapine is superior to placebo and at least equivalent to haloperidol for improving a broad range of symptoms encountered in patients with schizophrenia, including pos. symptoms, neg. symptoms, affective symptoms, and cognitive outcomes. Available data comparing quetiapine with other atypical antipsychotics, while limited, suggest it is as efficacious as other atypical agents and has a favorable tolerability profile; in particular, the incidence of motor adverse effects and prolactin elevation is comparable to that of placebo across its entire dose range. The favorable overall effectiveness of quetiapine suggests it is well suited for the long-term treatment of patients with psychotic disorders.

IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quetiapine in treatment of schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

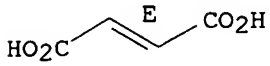


CM 2

CRN 110-17-8
CMF C4 H4 O4

QUETIAPINE

Double bond geometry as shown.



REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 17 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:376611 CAPLUS
DOCUMENT NUMBER: 138:374195
TITLE: Method for improving dissolution of poorly dispersible drugs
INVENTOR(S): Yamaguchi, Hisami; Saka, Shuji; Ueda, Takao
PATENT ASSIGNEE(S): Fujisawa Pharmaceutical Co., Ltd., Japan
SOURCE: PCT Int. Appl., 19 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003039516	A1	20030515	WO 2002-JP11315	20021030
W: JP, US				
RW: AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR				
EP 1448169	A1	20040825	EP 2002-788593	20021030
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, CY, TR, BG, CZ, EE, SK				
JP 3624954	B1	20050302	JP 2003-541807	20021030
US 2005003001	A1	20050106	US 2004-491887	20040415
JP 2004285075	A2	20041014	JP 2004-154569	20040525

PRIORITY APPLN. INFO.:

JP 2001-341435	A	20011107
JP 2001-314435	A	20011107
JP 2003-541807	A3	20021030
WO 2002-JP11315	W	20021030

AB The present invention is to provide a method for improving the dissoln. of a poorly dispersible drug and that is achieved by preparing a granulated product whereby a floating agent is added to the poorly dispersible drug. Thus, quetiapine fumarate 230.26, lactose 81.74, HPC 8, and cellulose 80 g were mixed and 130 mL EtOH was added to give the granules.

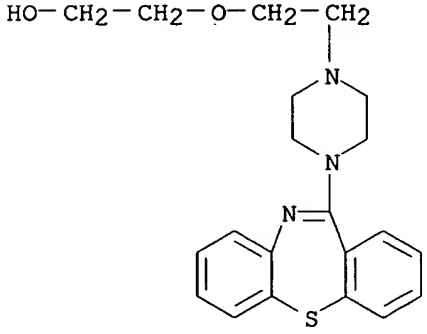
IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method for improving dissoln. of poorly dispersible drugs)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

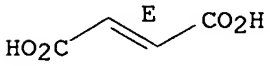


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 18 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:370518 CAPLUS
DOCUMENT NUMBER: 139:79025
TITLE: Efficacy and tolerability of quetiapine in patients with schizophrenia switched from other antipsychotics
AUTHOR(S): De Nayer, A.; Windhager, E.; Irmansyah; Larmo, I.; Lindenbauer, B.; Rittmannsberger, H.; Platz, T.; Jones, A. M.; Whiteford, J. L.; Altman, C. A.
CORPORATE SOURCE: SPECTRUM Study Group, Hopital Ste-Therese, Belg.
SOURCE: International Journal of Psychiatry in Clinical Practice (2003), 7(1), 59-66
CODEN: IJPCFZ; ISSN: 1365-1501
PUBLISHER: Martin Dunitz Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Objective: The Seroquel Patient Evaluation on Changing Treatment Relative to Usual Medication (SPECTRUM) study assessed the efficacy and tolerability of quetiapine (Seroquel) in patients with schizophrenia switched from treatments providing suboptimal outcomes. Methods: This was an international, open-label, non-comparative study, designed with titration to 400 mg/day quetiapine over 7 days, then flexible dosing (300-750 mg/day) for 11 wk. Efficacy was assessed with the Pos. and Neg. Syndrome Scale (PANSS); Clin. Global Impression (CGI) Severity of Illness and Global Improvement scores; and the Calgary Depression Scale for Schizophrenia (CDSS). Clin. benefit and tolerability were also assessed. Results: The mean modal dose of quetiapine was 505 mg/day; 509 patients switched to quetiapine from olanzapine (13%), risperidone (11%), conventional antipsychotics (37%) and combinations of antipsychotics (28%), amongst others. Significant decreases in CGI Severity of Illness and PANSS scores and a significant improvement in CDSS score resulted from the switch (all $P < 0.001$ vs. baseline). There were significant redns. in extrapyramidal symptoms (EPS) on the Simpson-Angus Scale (SAS) and Barnes Akathisia Scale (BAS) (both $P < 0.001$ vs. baseline) and a low incidence of EPS-related adverse events (4.7%). Conclusion: Results indicate that switching to quetiapine was clin. beneficial for patients with poor efficacy or intolerable side effects on their previous antipsychotic medication.

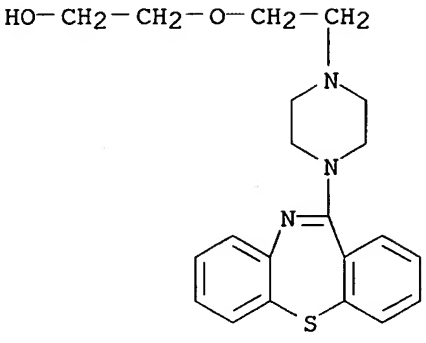
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(efficacy and tolerability of quetiapine in patients with schizophrenia switched from other antipsychotics)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

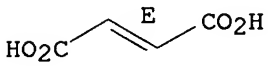
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 26 THERE ARE 26 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 19 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:202410 CAPLUS
DOCUMENT NUMBER: 138:226705
TITLE: Novel pharmaceuticals comprising drug conjugates with polypeptide carriers
INVENTOR(S): Picariello, Thomas
PATENT ASSIGNEE(S): New River Pharmaceuticals Inc., USA
SOURCE: PCT Int. Appl., 2059 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003020200	A2	20030313	WO 2001-US43117	20011116
WO 2003020200	A3	20030912		
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RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
CA 2429345	AA	20030313	CA 2001-2429345	20011116
EP 1357928	A2	20031105	EP 2001-273387	20011116
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				

PRIORITY APPLN. INFO.:		
US 2000-248600P	P	20001116
US 2000-248601P	P	20001116
US 2000-248603P	P	20001116
US 2000-248604P	P	20001116
US 2000-248606P	P	20001116
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US 2000-248711P	P	20001116

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US 2001-248774P	P	20011116
US 2001-248775P	P	20011116
US 2001-248778P	P	20011116
US 2001-248780P	P	20011116
US 2001-248781P	P	20011116
US 2001-248783P	P	20011116
US 2001-248784P	P	20011116
US 2001-248785P	P	20011116
US 2001-248786P	P	20011116
US 2001-248787P	P	20011116
US 2001-248790P	P	20011116
US 2001-248791P	P	20011116
US 2001-248792P	P	20011116
US 2001-248793P	P	20011116
US 2001-248833P	P	20011116
US 2001-248848P	P	20011116
US 2001-248849P	P	20011116
WO 2001-US43117	W	20011116

AB A pharmaceutical composition comprising a polypeptide and an active agent attached to said polypeptide is disclosed.

IT **111974-72-2D**, Quetiapine fumarate, polypeptide conjugates
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(novel pharmaceuticals comprising drug conjugates with polypeptide carriers)

RN 111974-72-2 CAPLUS

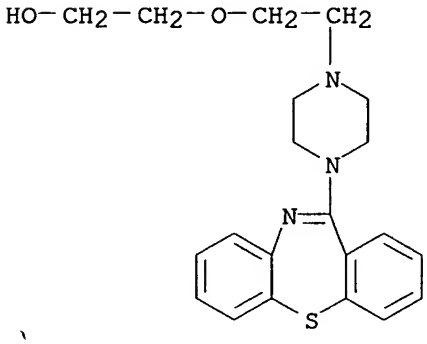
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-,

QUETIAPINE

(2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

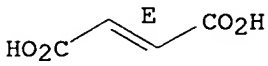
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 20 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:173425 CAPLUS
DOCUMENT NUMBER: 138:210343
TITLE: A pharmaceutical combination of quetiapine and zolmitriptan
INVENTOR(S): Lee, David
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2003018009	A1	20030306	WO 2002-SE1507	20020823
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
EP 1423112	A1	20040602	EP 2002-760969	20020823
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK				
JP 2005503391	T2	20050203	JP 2003-522527	20020823
US 2005020571	A1	20050127	US 2004-487701	20040920
PRIORITY APPLN. INFO.:			SE 2001-2855 A	20010827
			WO 2002-SE1507 W	20020823

AB The present invention relates to a combination comprising quetiapine or a pharmaceutically acceptable salt thereof and zolmitriptan or a pharmaceutically acceptable salt thereof, pharmaceutical compns., processes for its preparation, the use thereof in the manufacture of a medicament and a method of treatment of disease and more particularly to a method of treatment of diseases typically treated with 5-HT 1D agonists and/or atypical antipsychotics, in particularly, migraine, related conditions and for reducing or eliminating of migraine recurrence. Formulation of a tablet containing quetiapine fumarate 28, and zolmitriptan 5 mg is disclosed.

IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical combination of quetiapine and zolmitriptan)

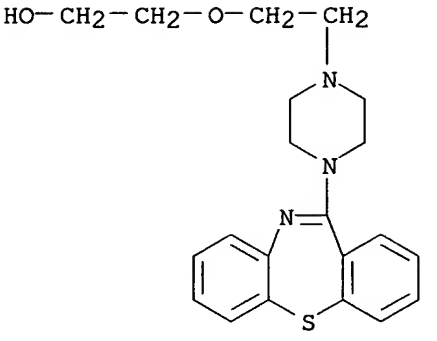
RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

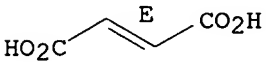
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 21 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2003:19961 CAPLUS
DOCUMENT NUMBER: 138:78464
TITLE: Pharmaceutical preparations based on active ingredients susceptible to illicit administration
INVENTOR(S): Garavani, Alberto; Marchiorri, Maurizio; Di Martino, Alessandro
PATENT ASSIGNEE(S): Altergon S.A., Switz.
SOURCE: Eur. Pat. Appl., 11 pp.
CODEN: EPXXDW
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
EP 1273301	A2	20030108	EP 2002-15073	20020705
EP 1273301	A3	20030409		

R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK

PRIORITY APPLN. INFO.: IT 2001-MI11446 A 20010706

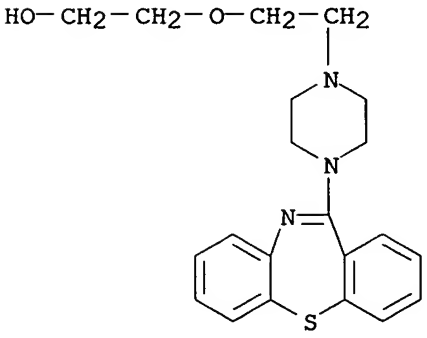
AB Disclosed are pharmaceutical formulations for oral administration, preferably in the form of a soft capsule enclosing an active principle susceptible to illicit administration and at least one pharmaceutically acceptable organoleptic marker which is particularly evident for its odor, taste or color or for its scarce miscibility with food. The active principle is selected from the group consisting of a substance acting on the central nervous system and/or as a narcotic and of a substance with anabolizing activity or the like. The organoleptic marker is independently selected out of one or more substances belonging to the group consisting of flavoring agents, flavoring agents, coloring agents, odorants, and oils.

IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(pharmaceutical prepns. based on active ingredients susceptible to illicit administration containing organoleptic markers)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

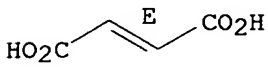


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 22 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:977588 CAPLUS
DOCUMENT NUMBER: 138:33362
TITLE: Use of cyclooxygenase 2 (COX-2) inhibitors for the treatment of schizophrenia, delusional disorders, affective disorders, autism, or tic disorders
INVENTOR(S): Muller, Norbert
PATENT ASSIGNEE(S): Germany
SOURCE: PCT Int. Appl., 58 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002102297	A2	20021227	WO 2002-EP6013	20020531
WO 2002102297	A3	20030501		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
DE 10129320	A1	20030410	DE 2001-10129320	20010619
EP 1397145	A2	20040317	EP 2002-738138	20020531
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004534066	T2	20041111	JP 2003-504886	20020531
US 2004204469	A1	20041014	US 2004-480600	20040205
PRIORITY APPLN. INFO.:			DE 2001-10129320 A	20010619
			US 2002-364904P P	20020314
			WO 2002-EP6013 W	20020531

OTHER SOURCE(S): MARPAT 138:33362

AB The invention discloses the use of a COX-2 inhibitor for the treatment of psychiatric disorders, e.g. schizophrenia, delusional disorders, affective disorders, autism or tic disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders, depressive episodes, recurring depressive episodes, manic episodes and bipolar affective disorders. Moreover, the invention discloses the use of a COX-2 inhibitor, in particular celecoxib, in combination with a neuroleptic drug, in particular risperidone, or an antidepressant, for the treatment of psychiatric disorders such as schizophrenia, delusional disorders, affective disorders, autism or tic disorders.

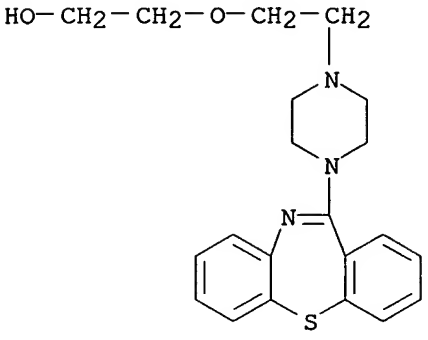
IT **111974-72-2**, Quetiapine fumarate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(cyclooxygenase 2 inhibitors for treatment of psychiatric disorders, and use with other agents)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

QUETIAPINE

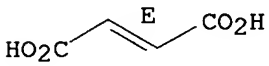
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 23 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:973398 CAPLUS
DOCUMENT NUMBER: 139:127856
TITLE: Discriminative stimulus properties in rats of the novel antipsychotic quetiapine
AUTHOR(S): Smith, Judith A.; Goudie, Andrew J.
CORPORATE SOURCE: Department of Psychology, Liverpool University, Liverpool, UK
SOURCE: Experimental and Clinical Psychopharmacology (2002), 10(4), 376-384
CODEN: ECLPES; ISSN: 1064-1297
PUBLISHER: American Psychological Association
DOCUMENT TYPE: Journal
LANGUAGE: English

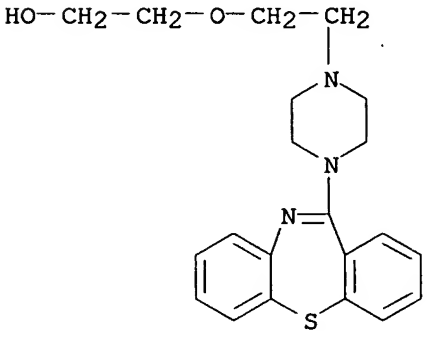
AB Rats discriminated the novel antipsychotic quetiapine (Seroquel). Full generalization was seen with the novel ("atypical") antipsychotics, clozapine, olanzapine, and risperidone. Generalization was not seen with the older "typical" antipsychotics, haloperidol, chlorpromazine, and loxapine, or with the novel atypical antipsychotic, amisulpride. The pattern of generalization resembled that seen in rats trained to discriminate a low dose (1.25 mg/kg) of clozapine, which dissocs. most novel antipsychotics from typical antipsychotics. However, the failure of the novel antipsychotic amisulpride to generalize demonstrates that this bioassay does not detect all novel antipsychotics. These data suggest that the discrimination of antipsychotics such as quetiapine may be of value in the development of novel antipsychotics, although the relationship between the discriminative properties of such drugs and their clin. actions is unclear.

IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); BIOL (Biological study)
(discriminative stimulus properties in rats of novel antipsychotic quetiapine compared with novel atypical and older typical antipsychotics)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



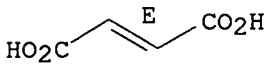
CM 2

CRN 110-17-8

QUETIAPINE

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 24 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:964929 CAPLUS
DOCUMENT NUMBER: 138:29170
TITLE: Transdermal and topical administration of antipsychotic agents using basic enhancers
INVENTOR(S): Luo, Eric C.; Hickey, Alan T. J.; Jacobson, Eric C.; Hsu, Tsung-Min
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 16 pp., Cont.-in-part of U.S. Ser. No. 972,008.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 25
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 2002192300	A1	20021219	US 2002-175681	20020619
US 2001051166	A1	20011213	US 2000-738410	20001214
US 6586000	B2	20030701		
US 2002018803	A1	20020214	US 2000-738395	20001214
US 6719997	B2	20040413		
US 2002034554	A1	20020321	US 2001-972008	20011004
US 6582724	B2	20030624		
ZA 2002004671	A	20030611	ZA 2002-4671	20020611

PRIORITY APPLN. INFO.:

US 1999-465098	A2	19991216
US 2000-569889	A2	20000511
US 2000-607892	B2	20000630
US 2000-738395	A2	20001214
US 2000-738410	A2	20001214
US 2001-972008	A2	20011004

AB Methods are provided for enhancing the permeability of skin or mucosal tissue to topical or transdermal application of antipsychotic agents. The methods entail the use of a base in order to increase the flux of the agent through a body surface while minimizing the likelihood of skin damage, irritation or sensitization. The permeation enhancer can be an inorg. or organic base. Compns. and transdermal systems are also described.

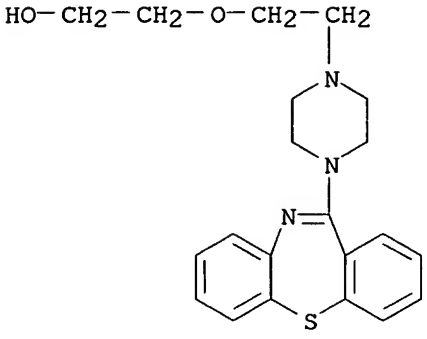
IT **111974-72-2,** Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(transdermal and topical administration of antipsychotic agents using basic enhancers)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

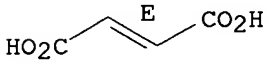
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 25 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:615412 CAPLUS
DOCUMENT NUMBER: 137:150254
TITLE: Method of treating substance abuse with quetiapine
INVENTOR(S): Brown, Sherwood
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002062346	A1	20020815	WO 2002-SE214		20020205
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
EP 1359919	A1	20031112	EP 2002-710643		20020205
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004518699	T2	20040624	JP 2002-562353		20020205
US 2004058910	A1	20040325	US 2003-470368		20030725
PRIORITY APPLN. INFO.:			US 2001-266808P	P	20010206
			WO 2002-SE214	W	20020205

AB This invention relates to a method of treating Substance Use such as Substance Abuse or Substance Dependence and in particular to the use of quetiapine in treating such disorders. Quetiapine was administered for 12 wk to 12 outpatients with bipolar disorder and cocaine dependence. Cocaine cravings significantly decreased. And, for the 8 subjects completing the study, there was an 87% reduction in amount spent on drugs. Tablet and capsule formulations are given.

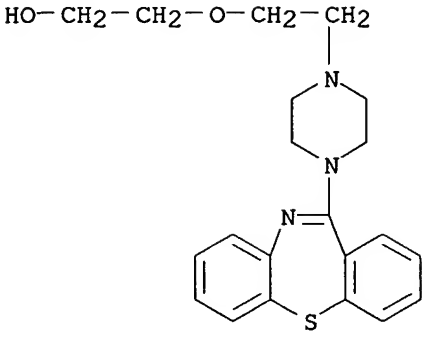
IT **111974-72-2**, Quetiapine fumarate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(method of treating substance abuse with quetiapine)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

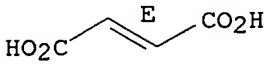
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 26 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:556104 CAPLUS
DOCUMENT NUMBER: 137:109489
TITLE: Compositions comprising a polypeptide and an active agent
INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J.
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 34 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
US 2002099013	A1	20020725	US 2001-933708		20010822
US 2004087483	A1	20040506	US 2002-136433		20020502
PRIORITY APPLN. INFO.:			US 2000-247556P	P	20001114
			US 2000-247558P	P	20001114
			US 2000-247559P	P	20001114
			US 2000-247560P	P	20001114
			US 2000-247561P	P	20001114
			US 2000-247594P	P	20001114
			US 2000-247595P	P	20001114
			US 2000-247606P	P	20001114
			US 2000-247607P	P	20001114
			US 2000-247608P	P	20001114
			US 2000-247609P	P	20001114
			US 2000-247610P	P	20001114
			US 2000-247611P	P	20001114
			US 2000-247612P	P	20001114
			US 2000-247620P	P	20001114
			US 2000-247621P	P	20001114
			US 2000-247634P	P	20001114
			US 2000-247635P	P	20001114
			US 2000-247698P	P	20001114
			US 2000-247699P	P	20001114
			US 2000-247700P	P	20001114
			US 2000-247701P	P	20001114
			US 2000-247702P	P	20001114
			US 2000-247797P	P	20001114
			US 2000-247798P	P	20001114
			US 2000-247799P	P	20001114
			US 2000-247800P	P	20001114
			US 2000-247801P	P	20001114
			US 2000-247802P	P	20001114
			US 2000-247803P	P	20001114
			US 2000-247804P	P	20001114
			US 2000-247805P	P	20001114
			US 2000-247807P	P	20001114
			US 2000-247832P	P	20001114
			US 2000-247833P	P	20001114
			US 2000-247926P	P	20001114
			US 2000-247927P	P	20001114
			US 2000-247928P	P	20001114
			US 2000-247929P	P	20001114
			US 2000-247930P	P	20001114
			US 2000-642820	A2	20000822
			US 2000-248607P	P	20001116

QUETIAPINE

US 2001-933708 A2 20010822

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

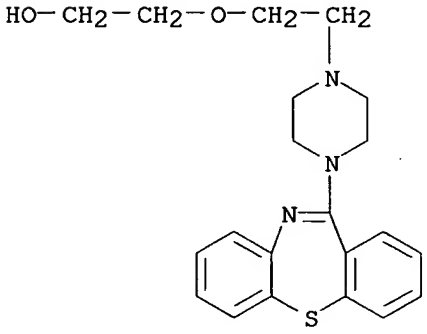
IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

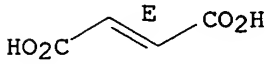
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 27 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:487405 CAPLUS
DOCUMENT NUMBER: 137:41768
TITLE: Quetiapine for treatment of dopaminergic therapy-associated dyskinesias, and combination for the treatment of Parkinson's disease
INVENTOR(S): Goldstein, Jeffrey
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2002049652	A1	20020627	WO 2001-SE2820		20011218
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG					
AU 2002016557	A5	20020701	AU 2002-16557		20011218
EP 1345610	A1	20030924	EP 2001-271220		20011218
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
JP 2004516271	T2	20040603	JP 2002-550992		20011218
US 2004058909	A1	20040325	US 2003-451171		20030620
PRIORITY APPLN. INFO.:			US 2000-287582P	P	20001220
			WO 2001-SE2820	W	20011218

AB A method for treating dyskinesias associated with dopaminergic therapy is described using the atypical antipsychotic agent quetiapine. Also described is the co-administration of quetiapine and a dopaminergic agent for treating Parkinson's disease. Treatment with quetiapine suppresses the symptoms of Parkinson's disease and will attenuate levodopa-induced dyskinetic movements. This allows the dosage of dopaminergic agents, e.g. levodopa, to be increased without the complicating side-effects normally observed with higher doses.

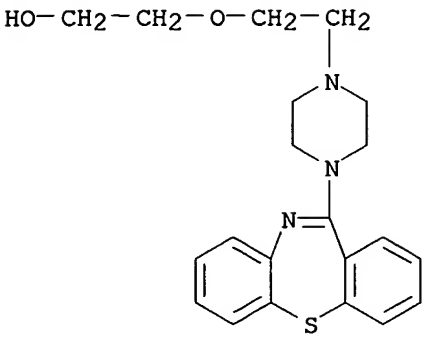
IT **111974-72-2**, Quetiapine fumarate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quetiapine for treatment of dopaminergic therapy-associated dyskinesias, and combination for treatment of Parkinson's disease)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

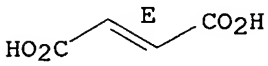
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 28 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:359684 CAPLUS
DOCUMENT NUMBER: 136:395303
TITLE: The effect of multiple doses of cimetidine on the steady-state pharmacokinetics of quetiapine in men with selected psychotic disorders
AUTHOR(S): Strakowski, Stephen M.; Keck, Paul E., Jr.; Wong, Y. W. James; Thyrum, Per T.; Yeh, Chiao
CORPORATE SOURCE: Bipolar and Psychotic Disorders Research Program, University of Cincinnati College of Medicine, OH, USA
SOURCE: Journal of Clinical Psychopharmacology (2002), 22(2), 201-205
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Quetiapine fumarate (Seroquel) is an atypical antipsychotic agent approved for the treatment of psychosis. It is extensively metabolized by the CYP450 3A4 isoenzyme. The principal aim of the study was to investigate the effect of multiple doses of cimetidine, a nonspecific P 450 inhibitor, on the steady-state pharmacokinetics of quetiapine. Thirteen patients (seven completers) with selected psychotic disorders received escalating doses of quetiapine from 25 to 150 mg three times daily on days 3 to 8 and were then maintained at 150 mg three times daily until day 19. Cimetidine (400 mg) was initiated on the afternoon of day 15 and administered three times daily with every dose of quetiapine thereafter. Quetiapine plasma concns. were measured before and after cimetidine coadministration, and quetiapine pharmacokinetic parameters were calculated Of the 13 men who entered the study, seven completed it. A slight increase in quetiapine plasma levels and reduction in oral clearance were observed after cimetidine coadministration. No serious adverse events were observed during quetiapine treatment. No clin. relevant alterations in quetiapine pharmacokinetics were observed after cimetidine coadministration in patients with psychotic disorders.

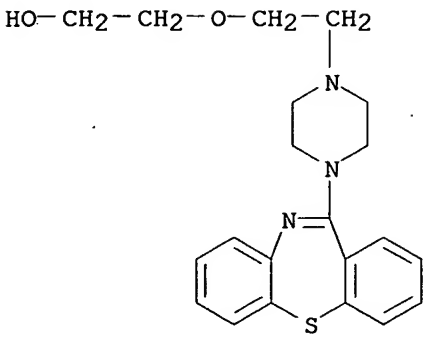
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of multiple doses of cimetidine on steady-state pharmacokinetics of quetiapine in men with selected psychotic disorders)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

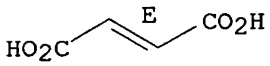
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 9 THERE ARE 9 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 29 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:359681 CAPLUS
DOCUMENT NUMBER: 137:178
TITLE: Effect of fluoxetine and imipramine on the pharmacokinetics and tolerability of the antipsychotic quetiapine
AUTHOR(S): Potkin, Steven G.; Thyrum, Per T.; Alva, Gustavo; Carreon, Danilo; Yeh, Chiao; Kalali, Amir; Arvanitis, Lisa A.
CORPORATE SOURCE: Department of Psychiatry and Human Behavior, University of California, Irvine, CA, USA
SOURCE: Journal of Clinical Psychopharmacology (2002), 22(2), 174-182
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of fluoxetine and imipramine on the pharmacokinetics and nonpsychiatric side effect profile of quetiapine fumarate were investigated in 26 patients with schizophrenia, schizoaffective disorder, or bipolar disorder in a multicenter, two-period, multiple-dose, open-label, randomized trial. Over a 1-to 2-wk period, patients were titrated to a 300-mg twice-daily dose of quetiapine. Patients treated for at least 7 days at the target dose entered a combination therapy period, receiving fluoxetine (60 mg daily) or imipramine (75 mg twice daily) for 8 days. Key assessments included pharmacokinetic anal. of quetiapine, the Udvalg for kliniske undersogelser (UKU) Side Effect Rating Scale, and safety evaluations (e.g., adverse events, electrocardiograms, laboratory tests, and vital signs). Fluoxetine increased the quetiapine area under the plasma concentration time curve during a 12-h interval (+ 12%), maximum plasma concentration during the dosing interval (Cssmax; +26%), and min. plasma concentration at the end of the dosing interval (+8%), although it decreased oral clearance (-11%). The change in Cssmax was statistically although not clin. significant. Imipramine did not affect the pharmacokinetics of quetiapine. Overall, scores on the UKU Side Effect Rating Scale improved during combination therapy with either agent, and no statistically significant deterioration was observed for any item. For safety assessments, the only clin. remarkable event was an imipramine-associated complete left bundle branch block in one patient. No unexpected side effects were reported. In conclusion, combination therapy with quetiapine and fluoxetine or imipramine had a minimal effect on quetiapine pharmacokinetics and was well tolerated.

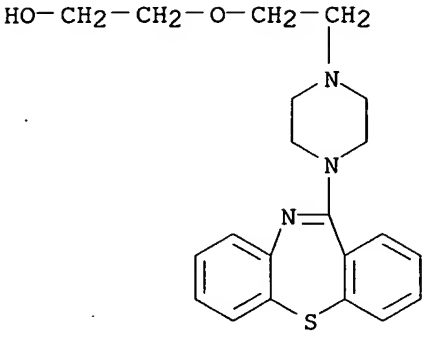
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of fluoxetine and imipramine on pharmacokinetics and tolerability of antipsychotic quetiapine)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

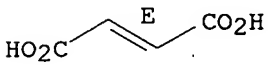
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 30 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:332011 CAPLUS
DOCUMENT NUMBER: 136:355482
TITLE: Compositions comprising a polypeptide and an active agent
INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J.
PATENT ASSIGNEE(S): New River Pharmaceuticals, Inc., USA
SOURCE: PCT Int. Appl., 98 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 12
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002034237	A1	20020502	WO 2001-US26142	20010822
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
US 6716452	B1	20040406	US 2000-642820	20000822
CA 2420590	AA	20020502	CA 2001-2420590	20010822
AU 2001086599	A5	20020506	AU 2001-86599	20010822
EP 1311242	A1	20030521	EP 2001-966056	20010822
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004523480	T2	20040805	JP 2002-537291	20010822
US 2004127397	A1	20040701	US 2003-727565	20031205
PRIORITY APPLN. INFO.:			US 2000-642820 A	20000822
			US 2000-247613P P	20001114
			US 2000-247614P P	20001114
			US 2000-247615P P	20001114
			US 2000-247616P P	20001114
			US 2000-247617P P	20001114
			US 2000-247622P P	20001114
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			US 2000-247631P P	20001114
			US 2000-247632P P	20001114
			US 2000-247633P P	20001114
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			US 2000-247606P P	20001114
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			US 2000-247609P P	20001114
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			US 2000-247611P P	20001114
			US 2000-247612P P	20001114
			US 2000-247620P P	20001114

US 2000-247621P	P	20001114
US 2000-247634P	P	20001114
US 2000-247635P	P	20001114
US 2000-247698P	P	20001114
US 2000-247699P	P	20001114
US 2000-247701P	P	20001114
US 2000-247702P	P	20001114
US 2000-247797P	P	20001114
US 2000-247798P	P	20001114
US 2000-247799P	P	20001114
US 2000-247800P	P	20001114
US 2000-247801P	P	20001114
US 2000-247802P	P	20001114
US 2000-247803P	P	20001114
US 2000-247804P	P	20001114
WO 2001-US26142	W	20010822

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

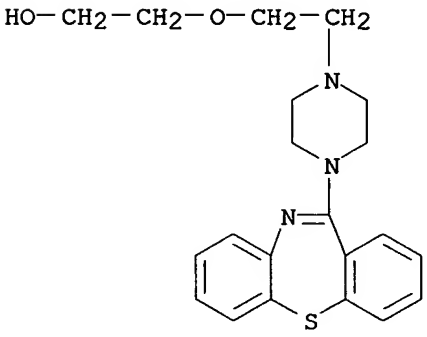
IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(compns. comprising a polypeptide and an active agent)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

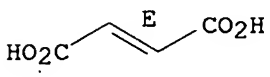
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 31 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:289828 CAPLUS
DOCUMENT NUMBER: 136:363155
TITLE: Dosing and switching strategies for quetiapine fumarate
AUTHOR(S): Cutler, Andrew J.; Goldstein, Jeffrey M.; Tumas, John A.
CORPORATE SOURCE: Coordinated Research of Florida, Inc, Winter Park, FL, USA
SOURCE: Clinical Therapeutics (2002), 24(2), 209-222
CODEN: CLTHDG; ISSN: 0149-2918
PUBLISHER: Excerpta Medica, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The atypical antipsychotic agent quetiapine fumarate has demonstrated efficacy and tolerability in clin. trials in patients with chronic or subchronic exacerbations of schizophrenic symptoms. This review summarizes clin. trial data and other practical information regarding the initiation and routine administration of quetiapine. Appropriate strategies for switching from other antipsychotic agents to quetiapine are also discussed. Quetiapine is an appropriate initial treatment for psychotic disturbances in patients with schizophrenia of any stage and for those in whom a therapeutic switch is indicated for clin. reasons, such as inability to tolerate the side effects of treatment. Titration to 400 mg/d is recommended using the following schedule, administered BID in divided doses: day 1, 50 mg; day 2, 100 mg; day 3, 200 mg; day 4, 300 mg; and day 5, 400 mg. In patients who respond to quetiapine, therapy should be continued at the optimal dose that maintains remission, within the range of 150 to 750 mg/d. When a change in therapy is indicated, several strategies for switching from one antipsychotic agent to another may be applied to switching to quetiapine. Whereas studies have shown that an abrupt switch to or withdrawal from quetiapine does not produce significant clin. consequences, in practice the switch should be carefully individualized to minimize the potential for psychotic relapse or development of withdrawal symptoms. Quetiapine has antipsychotic effects and good tolerability at doses from 150 to 750 mg/d. Patients can be switched to quetiapine and their treatment individualized to achieve the optimal therapeutic effect with a min. of dose-limiting side effects. There are several strategies for switching to quetiapine from another antipsychotic agent that do not appear to cause significant exacerbation of psychosis or withdrawal reactions.

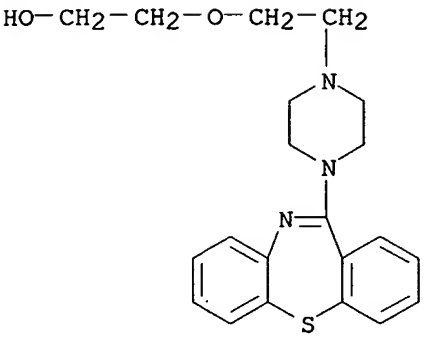
IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dosing and switching strategies for quetiapine fumarate in humans)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

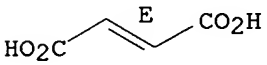
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 55 THERE ARE 55 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 32 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:237444 CAPLUS
DOCUMENT NUMBER: 137:288261
TITLE: A survey of some new drugs entering the field of commercial pharmaceutical compositions in 2001
AUTHOR(S): Masereel, Bernard
CORPORATE SOURCE: Dep. Pharmacie, FUNDP, Univ. Namur, Namur, 5000, Belg.
SOURCE: Journal de Pharmacie de Belgique (2002), 57(1), 1-13
CODEN: JPBEAJ; ISSN: 0047-2166
PUBLISHER: Association Pharmaceutique Belge, Service Scientifique
DOCUMENT TYPE: Journal; General Review
LANGUAGE: French

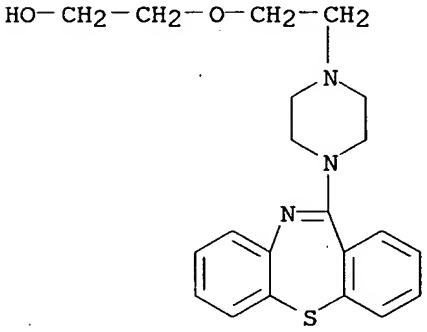
AB A review of new drugs which appeared on the Belgian market in 2001. Pharmacol. information on Plavix, Pariet, Nexiam, Uprima, Seroquel, Remergon, Reductil, Keppra, Reminyl, Yasmin, Novonorm, Avandia, and Actonel is provided.

IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); PKT (Pharmacokinetics); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new drugs in Belgium in 2001)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

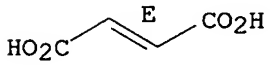
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 33 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:184906 CAPLUS
DOCUMENT NUMBER: 136:210599
TITLE: New use of quetiapine for treating attention deficit hyperactivity disorder and related disorders
INVENTOR(S): Robertson, John
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2002020019	A1	20020314	WO 2001-SE1879	20010831
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG				
AU 2001082832	A5	20020322	AU 2001-82832	20010831
EP 1326616	A1	20030716	EP 2001-961576	20010831
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2004508333	T2	20040318	JP 2002-524503	20010831
US 2004034010	A1	20040219	US 2003-398307	20030403
PRIORITY APPLN. INFO.:			SE 2000-3126 A	20000905
			WO 2001-SE1879 W	20010831

AB A method of treating Attention Deficit Hyperactivity Disorder, Conduct Disorder and related disorders which comprises using the atypical antipsychotic agent quetiapine. A 12-yr-old Caucasian male with conduct disorder and ADHD was successfully treated with quetiapine. Tablet and capsule formulations of quetiapine fumarate are given.

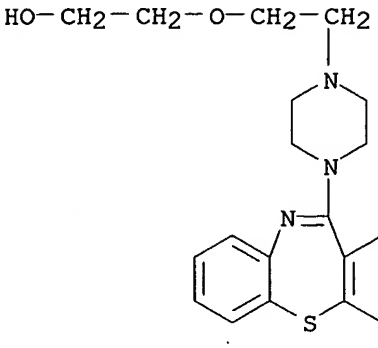
IT **111974-72-2**, Quetiapine fumarate
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(new use of quetiapine for treating attention deficit hyperactivity disorder and related disorders)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

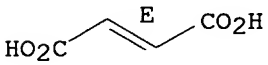
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 34 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2002:153684 CAPLUS
DOCUMENT NUMBER: 136:194261
TITLE: Therapeutic combinations of (S)-2-(benzylamino-methyl)-2,3,8,9,-tetrahydro 7H-1,4-dioxino{2,3-e}indol-8-one and neuroleptics for the treatment or prevention of psychotic disorders
INVENTOR(S): Marquis, Karen L.
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: U.S., 8 pp.
CODEN: USXXAM
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
US 6350773	B1	20020226	US 2000-728994	20001204
PRIORITY APPLN. INFO.:			US 1999-240908P P	19991210

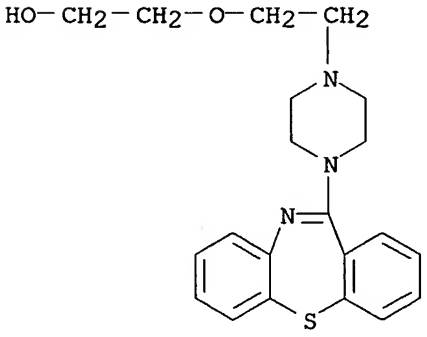
AB Therapeutic combinations useful in the treatment or prevention of psychotic disorders, to pharmaceutical compns. containing said combinations, and to their use in the treatment or prophylaxis of prevention disorders are provided. The effect of (S)-2-(benzylamino-methyl)-2,3,8,9-tetrahydro-7H-1,4-dioxino[2,3-e]indol-8-one on haloperidol-induced catalepsy in rats at 60 min after drug treatment was studied. A dose-dependent decrease in time spent in catalepsy position was observed A minimal ED of 0.3 mg/kg and an ED50 (dose producing 50% reduction in maximal response) of 0.08 mg/kg were calculated from these results.

IT **111974-72-2,** Seroquel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(therapeutic combinations of benzylaminotetrahydrodioxinoindolone and neuroleptics for treatment or prevention of psychotic disorders)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

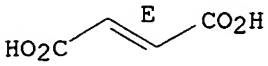


CM 2

QUETIAPINE

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 35 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:834747 CAPLUS
DOCUMENT NUMBER: 136:112575
TITLE: Quetiapine alone and added to a mood stabilizer for serious mood disorders
AUTHOR(S): Sajatovic, Martha; Brescan, Debra W.; Perez, Dalia E.; DiGiovanni, Sue K.; Hattab, Helen; Ray, Joan Belton; Bingham, C. Raymond
CORPORATE SOURCE: Department of Psychiatry, Case Western Reserve University, Cleveland, OH, USA
SOURCE: Journal of Clinical Psychiatry (2001), 62(9), 728-732
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Use of antipsychotic medication intermittently or over the long term may be necessary in treating patients with bipolar disorder whose symptoms have responded suboptimally to standard mood-stabilizing agents. Quetiapine fumarate is an effective novel antipsychotic with mixed serotonergic (5-HT2) and dopaminergic (D2) activity. This is an open-label, 12-wk prospective study to assess the efficacy and tolerability of quetiapine in the treatment of patients with bipolar and schizoaffective disorder who were suboptimally responsive to mood stabilizers alone. Participants in the study were inpatients or outpatients with a DSM-IV diagnosis of bipolar or schizoaffective disorder. Baseline psychopathol. was evaluated with the Brief Psychiatric Rating Scale (BPRS), the Young Mania Rating Scale (YMRS), and the Hamilton Rating Scale for Depression (HAM-D). Involuntary movements were rated with the Simpson-Angus Neurol. Rating Scale. Quetiapine was added on an open-label basis and increased to optimum clin. dosage. Psychopathol. and Abnormal Involuntary Movement Scale ratings were repeated weekly for the first 4 wk and then again at weeks 8 and 12. Ten individuals with bipolar disorder and 10 with schizoaffective disorder received quetiapine therapy. Overall, patients improved, with significant improvement in BPRS ($p < .001$), YMRS ($p = .043$), and HAM-D scores ($p = .002$). Simpson-Angus score also significantly decreased ($p = .02$). Overall, quetiapine was well tolerated by patients in this group with serious mood disorders. The mean ± SD quetiapine dose was 202.9±124.3 mg/day (range, 50-400 mg/day). Mean weight gain was 10.9 lb (4.9 kg). Although limited by its small size, open-label design, and relative gender homogeneity, this study suggests that quetiapine therapy may be useful in the treatment of individuals with serious mood disorders who are suboptimally responsive to mood stabilizers alone. These preliminary findings should be explored in larger, controlled trials.

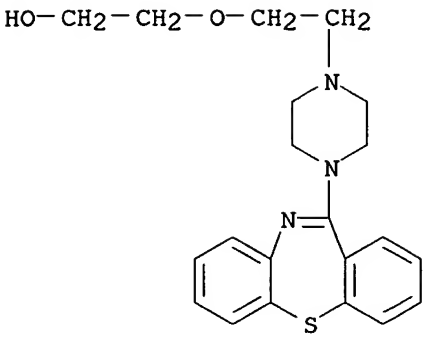
IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quetiapine alone and added to a mood stabilizer for serious mood disorders in humans)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

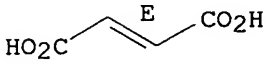
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 36 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:770605 CAPLUS
DOCUMENT NUMBER: 136:145053
TITLE: Cognitive improvements in psychotic subjects treated with "Seroquel" (quetiapine fumarate): an exploratory study
AUTHOR(S): Fleming, Kirsten; Thyrum, Per; Yeh, Chiao; Vargo, Dennis L.; Potkin, Steven G.
CORPORATE SOURCE: University of California, Irvine, CA, USA
SOURCE: Journal of Clinical Psychopharmacology (2001), 21(5), 527-529
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Lippincott Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

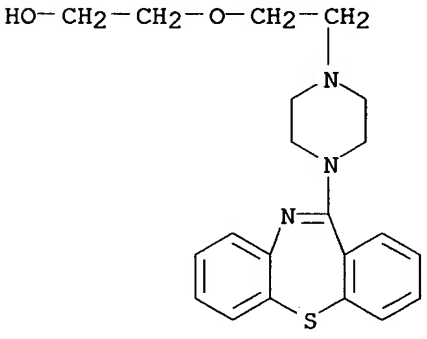
AB The effect of quetiapine treatment in male subjects with psychotic disorders was evaluated. Results showed that treatment with quetiapine significantly improved performance on Digit-Symbol Substitution, a measure involving attention and learning, and a trend of improvement on tests of motor speed, speed and set shift, and language measure. Quetiapine also produced improvement on a measure of executive function. The less binding activity of quetiapine to the dopamine D1-receptors, may possibly result in improvement on complex tasks.

IT **111974-72-2**, Seroquel
RL: PAC (Pharmacological activity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of quetiapine fumarate (Seroquel) on cognition in psychotic subjects)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

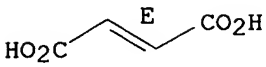


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 37 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:567099 CAPLUS
DOCUMENT NUMBER: 135:326843
TITLE: Atypical antipsychotics for schizophrenia: their collective role and comparative profiles
AUTHOR(S): Kennedy, Annette; Jain, Satyam; Vinogradov, Sophia
CORPORATE SOURCE: Department of psychiatry, University of California, San Francisco (UCSF), and San Francisco Department of Veterans Affairs Medical Center (VAMC), San Francisco, CA, 94122, USA
SOURCE: Formulary (2001), 36(7), 500-504,507,511-514,517
CODEN: FORMF9; ISSN: 1082-801X
PUBLISHER: Advanstar Communications, Inc.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

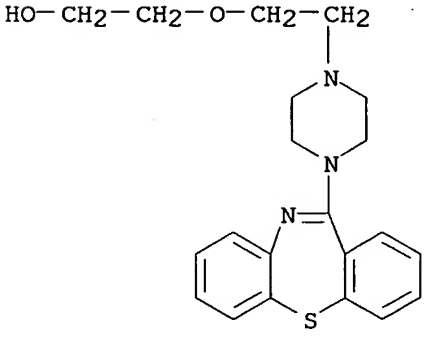
AB A review with refs. The novel or atypical antipsychotic medications introduced over the last decade represent a significant step forward in schizophrenia pharmacotherapy. While conventional antipsychotics effectively reduce psychotic symptoms, especially pos. symptoms, they often induce extrapyramidal system side effects and tardive dyskinesia. The atypical agents are generally free of these unwanted effects and generally have a more favorable adverse-effect profile than conventional antipsychotics. Moreover, in addition to effectively treating pos. psychotic symptoms, atypical agents are often helpful for patients unresponsive to conventional agents and may be more effective for neg. symptoms and cognitive dysfunction. Economic studies to date suggest that overall treatment costs are generally no higher with atypical antipsychotics relative to conventional antipsychotics despite the atypical agents' higher acquisition costs. This review profiles the five available atypical agents' (risperidone, olanzapine, clozapine, quetiapine, and ziprasidone) collective and individual roles, with an emphasis on each agent's advantages and disadvantages.

IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotics for schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

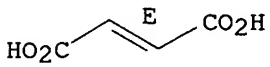


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



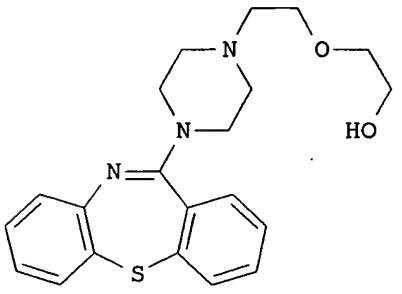
REFERENCE COUNT: 88 THERE ARE 88 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 38 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:565020 CAPLUS
DOCUMENT NUMBER: 135:137530
TITLE: A process for the preparation of quetiapine and its intermediates
INVENTOR(S): Bozsing, Daniel; Kovanyine, Lax Gyoergyi; Simig, Gyula; Rakoczy, Gyoergyne; Toempe, Peter; Krasznai, Gyoergy; Vereczkeyne, Donath Gyoergyi; Nagy, Kalman
PATENT ASSIGNEE(S): Egis Gyogyszergyar Rt., Hung.; Kovanyine Lax, Gyoergyi; Vereczkeyne Donath, Gyoergyi
SOURCE: PCT Int. Appl., 26 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
WO 2001055125	A1	20010802	WO 2001-HU10		20010124
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI					
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG					
EP 1252151	A1	20021030	EP 2001-904235		20010124
EP 1252151	B1	20040317			
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR					
AT 261949	E	20040415	AT 2001-904235		20010124
ES 2217115	T3	20041101	ES 2001-1904235		20010124
PRIORITY APPLN. INFO.:			HU 2000-283	A	20000125
			WO 2001-HU10	W	20010124

OTHER SOURCE(S): CASREACT 135:137530
GI



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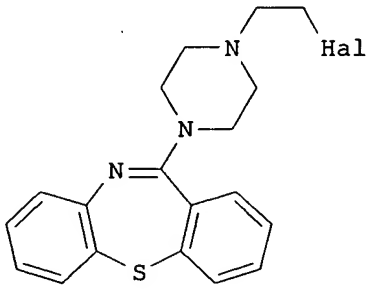


II

AB Novel process for the preparation of 11-{4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl}dibenzo[b,f]-1,4-thiazepine I (known as quetiapine), starting with Ph 2-phenylthiophenyl carbamate and 1-(2-hydroxyethyl)piperazine, was described. According to the invention, in the last step of synthesis, the haloethylpiperazinylthiazepine II is reacted with ethylene glycol.

IT **111974-72-2P**

QUETIAPINE

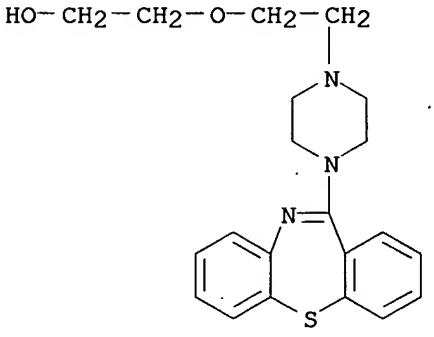
RL: IMF (Industrial manufacture); SPN (Synthetic preparation); PREP (Preparation)
(a process for the preparation of quetiapine and its intermediates)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

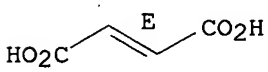
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 39 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:434851 CAPLUS
DOCUMENT NUMBER: 135:29153
TITLE: Therapeutic combinations of (S)-2-(benzylamino-methyl)-2,3,8,9,-tetrahydro-7H-1,4-dioxino[2,3-e]indol-8-one and neuroleptics for the treatment or prevention of psychotic disorders
INVENTOR(S): Marquis, Karen Lovell
PATENT ASSIGNEE(S): American Home Products Corporation, USA
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001041750	A2	20010614	WO 2000-US33060	20001207
WO 2001041750	A3	20020214		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2396351	AA	20010614	CA 2000-2396351	20001207
BR 2000016168	A	20020820	BR 2000-16168	20001207
EP 1235570	A2	20020904	EP 2000-982461	20001207
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR				
JP 2003516350	T2	20030513	JP 2001-543095	20001207
NZ 519381	A	20040430	NZ 2000-519381	20001207
NO 2002002739	A	20020607	NO 2002-2739	20020607
ZA 2002005484	A	20031009	ZA 2002-5484	20020709
PRIORITY APPLN. INFO.:			US 1999-458607 A	19991210
			WO 2000-US33060 W	20001207

AB Therapeutic combinations containing (S)-2-(benzylamino-methyl)-2,3,8,9,-tetrahydro-7H-1,4-dioxino[2,3-e]indol-8-one and an antipsychotic agent are provided which are useful in the treatment or prevention of psychotic disorders. Also provided are pharmaceutical compns. containing the combinations, and their therapeutic use.

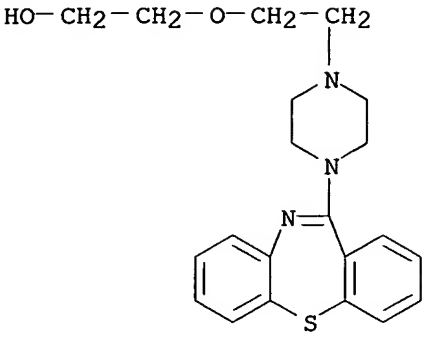
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(dioxinoindolone derivative-antipsychotic agent combination for treatment or prevention of psychotic disorder)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

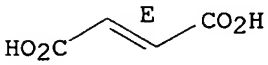
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 40 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:228713 CAPLUS
DOCUMENT NUMBER: 134:256881
TITLE: Quetiapine granules for tretament of diseases of the central nervous system
INVENTOR(S): Brown, Daniel Boyd
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.; Astrazeneca UK Limited
SOURCE: PCT Int. Appl., 16 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2001021179	A1	20010329	WO 2000-GB3598	20000918
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2383131	AA	20010329	CA 2000-2383131	20000918
TR 200200716	T2	20020621	TR 2002-200200716	20000918
EP 1218009	A1	20020703	EP 2000-960855	20000918
EP 1218009	B1	20050202		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
BR 2000014107	A	20020820	BR 2000-14107	20000918
JP 2003509461	T2	20030311	JP 2001-524605	20000918
EE 200200150	A	20030415	EE 2002-150	20000918
NZ 517549	A	20031031	NZ 2000-517549	20000918
AU 776292	B2	20040902	AU 2000-73023	20000918
ZA 2002001709	A	20030528	ZA 2002-1709	20020228
BG 106509	A	20021229	BG 2002-106509	20020311
NO 2002001394	A	20020320	NO 2002-1394	20020320
US 6599897	B1	20030729	US 2002-88804	20020321
US 2004228914	A1	20041118	US 2003-627198	20030725
PRIORITY APPLN. INFO.:			GB 1999-22271 A	19990921
			WO 2000-GB3598 W	20000918
			US 2002-88804 A1	20020321

AB Granule formulations of quetiapine and its salts and their use in treating diseases of the central nervous system such as psychotic disease conditions including schizophrenia are described. Thus, formulation contained Quetiapine fumarate 28.8, maltodextrin 950.0, aspartame 21.2 and water qs 186.0 mg/dose. The fumarate salt was equivalent to 86.8% free base.

IT **111974-72-2**, Quetiapine fumarate
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quetiapine granules for tretament of diseases of central nervous system)

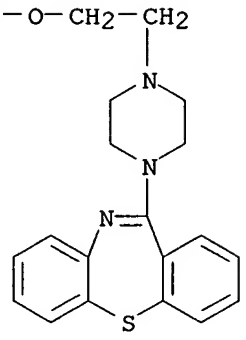
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7

QUETIAPINE

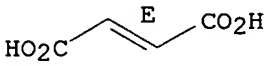
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 41 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:70664 CAPLUS
DOCUMENT NUMBER: 135:132202
TITLE: The long-term effect of quetiapine (Seroquel) monotherapy on weight in patients with schizophrenia
AUTHOR(S): Brecher, M.; Rak, I. W.; Melvin, K.; Jones, A. M.
CORPORATE SOURCE: AstraZeneca, Wilmington, DE, USA
SOURCE: International Journal of Psychiatry in Clinical Practice (2000), 4(4), 287-291
CODEN: IJPCFZ; ISSN: 1365-1501
PUBLISHER: Martin Dunitz Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB INTRODUCTION: Quetiapine (Seroquel) is an atypical antipsychotic drug with demonstrated efficacy and tolerability. In particular, placebo level extrapyramidal symptoms (EPS) across the entire dose range and a low propensity to cause sexual dysfunction suggest it may be associated with greater patient acceptability than alternative treatments. However, other side-effects, such as weight gain, may also have a significant impact on treatment acceptability. METHOD: We report the long-term weight changes observed in a cohort of 427 patients with schizophrenia from controlled and open-label extension (OLE) trials, in which quetiapine (mean dose 475 mg/day after 1 yr) was the only antipsychotic medication during the OLE period. RESULTS: In these patients, there was no overall effect on weight across the body mass index (BMI) spectrum. There were no dose-related effects on weight, and only one patient withdrew from treatment due to an adverse event of weight gain. Quetiapine appeared to have a weight neutral or 'normalizing' effect, with a tendency towards favorable shifts in bodyweight in underweight patients (BMI < 18.5 kg/m2) and severely obese patients (BMI ≥ 35 kg/m2). CONCLUSION: These results indicate that long-term weight changes with quetiapine monotherapy are minimal and potentially beneficial, and do not appear to raise the medical concerns associated with some other atypical agents.

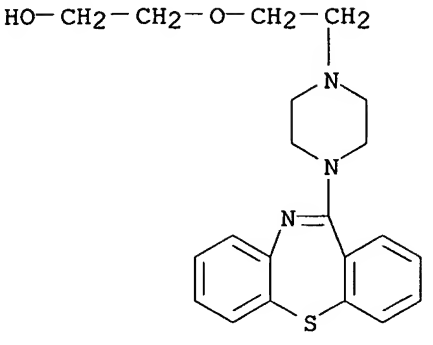
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(long-term effect of quetiapine (Seroquel) monotherapy on weight in humans with schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

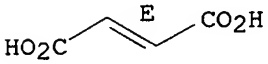
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 23 THERE ARE 23 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 42 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2001:6274 CAPLUS
DOCUMENT NUMBER: 134:216805
TITLE: Behavioral Approach to Nondyskinetic Dopamine Antagonists: Identification of Seroquel
AUTHOR(S): Warawa, Edward J.; Migler, Bernard M.; Ohnmacht, Cyrus J.; Needles, Ann L.; Gatos, George C.; McLaren, Frances M.; Nelson, Cynthia L.; Kirkland, Karen M.
CORPORATE SOURCE: Departments of Medicinal Chemistry Pharmacology and Drug Disposition and Metabolism, AstraZeneca Pharmaceuticals LP, Wilmington, DE, 19850-5437, USA
SOURCE: Journal of Medicinal Chemistry (2001), 44(3), 372-389
CODEN: JMCMAR; ISSN: 0022-2623
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A great need exists for antipsychotic drugs which will not induce extrapyramidal symptoms (EPS) and tardive dyskinesias (TDs). These side effects are deemed to be a consequence of nonselective blockade of nigrostriatal and mesolimbic dopamine D2 receptors. Nondyskinetic clozapine (1) is a low-potency D2 dopamine receptor antagonist which appears to act selectively in the mesolimbic area. In this work dopamine antagonism was assessed in two mouse behavioral assays: antagonism of apomorphine-induced climbing and antagonism of apomorphine-induced disruption of swimming. The potential for the liability of dyskinesias was determined in haloperidol-sensitized Cebus monkeys. Initial examination of a few close congeners of 1 enhanced confidence in the Cebus model as a predictor of dyskinetic potential. Among dibenzodiazepines, 1 did not induce dyskinesias whereas its N-2-(2-hydroxyethoxy)ethyl analog was dyskinetic. The emergence of such distinctions presented an opportunity. Thus, aromatic and N-substituted analogs of 6-(piperazin-1-yl)-11H-dibenz[b,e]azepines and 11-(piperazin-1-yl)dibenzo[b,f][1,4]thiazepines and -oxazepines were prepared and evaluated. 11-(4-[2-(2-Hydroxyethoxy)ethyl]piperazin-1-yl)dibenzo[b,f][1,4]thiazepine was found to be an apomorphine antagonist comparable to clozapine. It was essentially nondyskinetic in the Cebus model. A number of N-substituted analogs were found to be good apomorphine antagonists but all were dyskinetic.

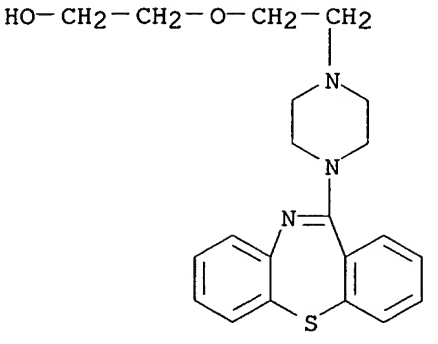
IT **111974-72-2P**
RL: SPN (Synthetic preparation); PREP (Preparation)
(preparation of piperazinyl dibenzazepines as nondyskinetic dopamine antagonists)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

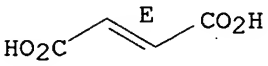
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 43 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:883892 CAPLUS
DOCUMENT NUMBER: 135:70580
TITLE: Prediction of the outcome of a phase 3 clinical trial of an antischizophrenic agent (quetiapine fumarate) by simulation with a population pharmacokinetic and pharmacodynamic model
AUTHOR(S): Kimko, Hui C.; Reele, Stots S. B.; Holford, Nicholas H. G.; Peck, Carl C.
CORPORATE SOURCE: Center for Drug Development Science, Georgetown University Medical Center, Washington, DC, 20007, USA
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis) (2000), 68(5), 568-577
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A completed phase 3 trial result was simulated 100 times on the basis of a simulation model of quetiapine fumarate (Seroquel), an antischizophrenic agent. The simulation was executed by analysts who were completely blinded from results of the actual trial until after the simulations were submitted to the holder of the trial results. Data from two clin. investigation of quetiapine in patients with schizophrenia were analyzed by use of nonlinear mixed effects modeling to derive a population pharmacokinetic- and pharmacodynamic-based simulation model. The time course of quetiapine concns. was described by use of a one-compartment open linear pharmacokinetic model with first-order absorption and elimination. The combination of an inhibitory maximum effect pharmacodynamic model for the active treatment effect and a linear function of time for the placebo effect characterized the observed time course of change in the Brief Psychiatric Rating Scale. Simulation results were compared with those in the actual trial to evaluate how well the simulations predicted the outcome. The actual trial results for all doses except the placebo group fell within the predicted Brief Psychiatric Rating Scale scores ± 1 SE. Unlike the phase 2 trial, from which the pharmacokinetic/pharmacodynamic model was developed, the placebo group in the actual phase 3 trial showed deterioration of Brief Psychiatric Rating Scale scores with time. We conclude that variable placebo responses observed in short-term studies of schizophrenia provide an inadequate basis for the modeling and simulation of placebo subjects in clin. trials. Knowledge of the range of placebo response observed in other studies may have provided an improved basis for the placebo effect model. The model for active drug produced adequate predictions of the actual trial outcomes.

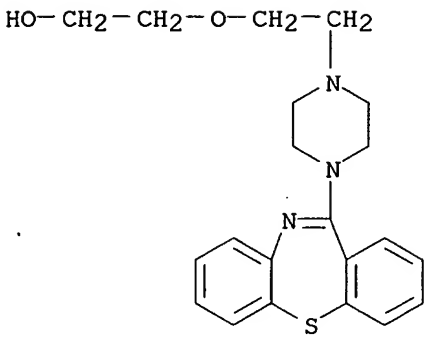
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmacokinetic/pharmacodynamic model for antischizophrenic agent (quetiapine fumarate) in humans)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

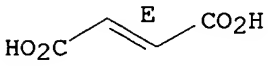
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 44 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:883040 CAPLUS
DOCUMENT NUMBER: 135:144
TITLE: Atypical antipsychotics: modelling and QSAR
AUTHOR(S): Tehan, Benjamin G.; Wong, Margaret G.; Cross, Graeme J.; Lloyd, Edward J.
CORPORATE SOURCE: Chemistry Department, Swinburne University of Technology, 3122, Australia
SOURCE: Molecular Modeling and Prediction of Bioactivity, [Proceedings of the European Symposium on Quantitative Structure-Activity Relationships: Molecular Modeling and Prediction of Bioactivity], 12th, Copenhagen, Denmark, Aug. 23-28, 1998 (2000), Meeting Date 1998, 448-449. Editor(s): Gundertofte, Klaus; Jorgensen, Flemming Steen. Kluwer Academic/Plenum Publishers: New York, N. Y.
CODEN: 69ASO3
DOCUMENT TYPE: Conference
LANGUAGE: English

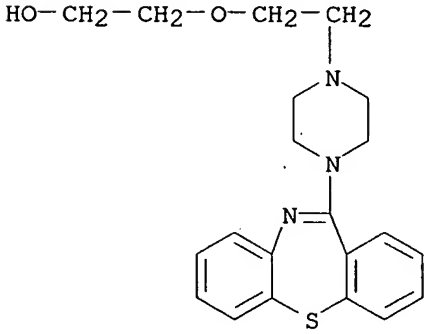
AB Antipsychotic drugs may be defined as medications that alleviate delusions, hallucinations and some aspects of formal thought disorder that occur in a variety of illnesses, most notably schizophrenia. The mechanism of action of these drugs has focused on their interaction with the central nervous system (CNS) neurotransmitter dopamine (DA). However, recent studies strongly implicate the neurotransmitter serotonin (5HT) as a further target of action. Antipsychotic drugs are further loosely classified into typical or atypical, initially based on animal model tests. A set of ligands ((R)- and (S)-octoclothepin, clozapine, Org5222, seroquel, olanzapine, sertindole, risperidone, ziprasidone, zotepine, remoxipride, loxapine) with high affinity for D2 and 5HT2A and classified as atypical and typical antipsychotics were selected for pharmacophore mapping. Further studies were carried out on sertindole, risperidone, zotepine, ziprasidone and haloperidol once a pharmacophore model has been established.

IT **111974-72-2**, Seroquel
RL: PRP (Properties); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(mol. modeling and QSAR for atypical antipsychotics)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

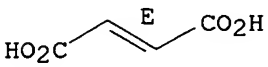


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 45 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:861473 CAPLUS
DOCUMENT NUMBER: 134:32972
TITLE: Porous drug matrixes containing polymers and sugars and methods of their manufacture
INVENTOR(S): Straub, Julie; Bernstein, Howard; Chickering, Donald E., III; Khatak, Sarwat; Randall, Greg
PATENT ASSIGNEE(S): Acusphere, Inc., USA
SOURCE: PCT Int. Appl., 45 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000072827	A2	20001207	WO 2000-US14578	20000525
WO 2000072827	A3	20010125		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6395300	B1	20020528	US 1999-433486	19991104
CA 2371836	AA	20001207	CA 2000-2371836	20000525
EP 1180020	A2	20020220	EP 2000-939365	20000525
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 2000010984	A	20020430	BR 2000-10984	20000525
JP 2003500438	T2	20030107	JP 2000-620939	20000525
NZ 516083	A	20030829	NZ 2000-516083	20000525
AU 768022	B2	20031127	AU 2000-54459	20000525
US 2002041896	A1	20020411	US 2001-798824	20010302
US 6610317	B2	20030826		
NO 2001005753	A	20020128	NO 2001-5753	20011126
ZA 2001010347	A	20030730	ZA 2001-10347	20011218

PRIORITY APPLN. INFO.:		
US 1999-136323P	P	19990527
US 1999-158659P	P	19991008
US 1999-433486	A	19991104
US 2000-186310P	P	20000302
WO 2000-US14578	W	20000525

AB Drugs, especially low aqueous solubility drugs, are provided in a porous matrix form, preferably microparticles, which enhances dissoln. of the drug in aqueous media. The drug matrixes preferably are made using a process that includes (i) dissolving a drug, preferably a drug having low aqueous solubility, in a volatile solvent to form a drug solution, (ii) combining at least one pore forming agent with the drug solution to form an emulsion, suspension, or second solns., and (iii) removing the volatile solvent and pore forming agent from the emulsion, suspension, or second solution to yield the porous matrix of drug. The pore forming agent can be either a volatile liquid that is immiscible with the drug solvent or a volatile solid compound, preferably a volatile salt. In a preferred embodiment, spray drying is used to remove the solvents and the pore forming agent. The resulting porous matrix has a faster rate of dissoln. following administration to a

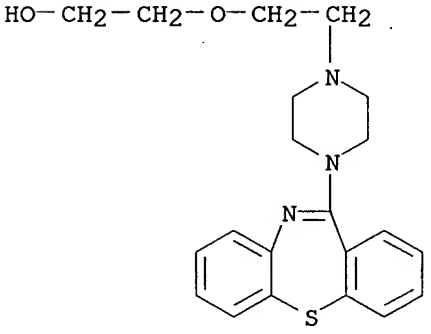
patient, as compared to non-porous matrix forms of the drug. In a preferred embodiment, microparticles of the porous drug matrix are reconstituted with an aqueous medium and administered parenterally, or processed using standard techniques into tablets or capsules for oral administration. Paclitaxel or docetaxel can be provided in a porous matrix form, which allows the drug to be formulated without solubilizing agents and administered as a bolus. For example, a nifedipine-loaded organic solution was prepared by dissolving 9.09 g of PEG 3350, 2.27 g of nifedipine, and 0.009 g of lecithin in 182 mL of methylene chloride. An aqueous solution was prepared by dissolving 3.27 g of NH4HCO3 and 0.91 g of PEG 3350 in 1.82 mL of water. The aqueous and organic solns. were homogenized and resulting emulsion was spray dried. A suspension of the porous nifedipine drug matrix was prepared in 5% dextrose solution at a concentration of 2.5 mg/mL. A bolus injection of the suspension was tolerated when administrated to dogs.

IT **111974-72-2**, Quetiapine fumarate
RL: PEP (Physical, engineering or chemical process); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(preparation of porous matrixes containing hydrophilic polymers and sugars for enhancement of drug dissoln.)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

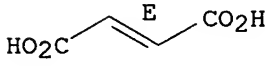
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 46 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:841965 CAPLUS
DOCUMENT NUMBER: 134:535
TITLE: Method of treatment
INVENTOR(S): Reinstein, Michael J.; Jones, Andrew Martin
PATENT ASSIGNEE(S): Astrazeneca AB, Swed.
SOURCE: PCT Int. Appl., 9 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000071106	A2	20001130	WO 2000-GB1875	20000516
WO 2000071106	A3	20020510		
W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2363784	AA	20001130	CA 2000-2363784	20000516
EP 1223939	A1	20020724	EP 2000-927593	20000516
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL				
JP 2003500353	T2	20030107	JP 2000-619413	20000516

PRIORITY APPLN. INFO.:		
GB 1999-11499	A	19990519
GB 2000-2762	A	20000208
WO 2000-GB1875	W	20000516

AB A method of treating weight in patients, in particular those suffering from psychoses, by administering the antipsychotic agent quetiapine.

IT **111974-72-2**, Quetiapine fumarate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treatment of weight gain in patients with antipsychotic quetiapine)

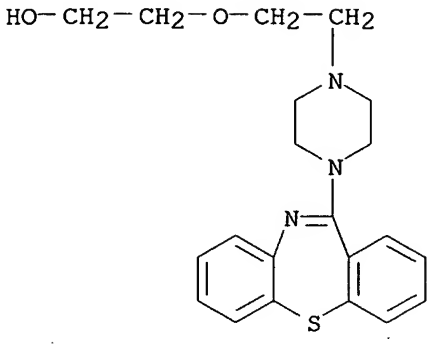
RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

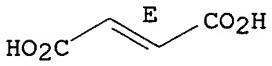
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 47 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:587824 CAPLUS
DOCUMENT NUMBER: 134:36915
TITLE: Quetiapine fumarate overdose: clinical and pharmacokinetic lessons from extreme conditions
AUTHOR(S): Pollak, P. Timothy; Zbuk, Kevin
CORPORATE SOURCE: Department of Medicine, Queen Elizabeth II HSC, Dalhousie University, Halifax, NS, Can.
SOURCE: Clinical Pharmacology & Therapeutics (St. Louis) (2000), 68(1), 92-97
CODEN: CLPTAT; ISSN: 0009-9236
PUBLISHER: Mosby, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Background: Although the new atypical antipsychotic, quetiapine fumarate, is growing in popularity over its progenitor, clozapine, clin. experience with overdose of this agent remains limited. Observation of an overdose situation provided a unique opportunity to define the safety, clin. effects, and pharmacokinetics of this medication more clearly. Methods: A patient admitted immediately after ingesting an overdose of 30 tablets of 100 mg of quetiapine was observed carefully to document effects of the medication. These observations were compared with the only two other published cases of overdose, to the known pharmacol. of the drug, and to serial measurements of serum drug concns. obtained to document the time course of elimination of the drug. Results: Consistent with the two previously published cases, the main clin. effects of overdose were hypotension, tachycardia, and somnolence as predicted by its known α-adrenergic receptor and histamine receptor blockade. These effects were managed with fluid resuscitation and supportive measures. No cardiac arrhythmias other than tachycardia have been reported, but the tachycardia was of an unexpectedly long duration in this case. Decline in serum quetiapine concentration followed a biexponential pattern with a terminal elimination half-life of 22 h. Unexpectedly low peak serum concns. in three patients with overdose suggest that absorption is highly reduced, either by the effects of the overdose or by the activated charcoal administered. Conclusions: Quetiapine appears to have greater safety in overdose than traditional antipsychotic agents. Its toxicity is consistent with its receptor pharmacol. Elevated serum concns. associated with this overdose remained above the limit of detection long enough to document a terminal elimination half-life of 22 h in this patient. This is much more consistent with previously noted duration of clin. effects and detectable serum concns. after overdose than the published half-life of 6 h. Physicians should be aware that any new drug that is active at low concns. may have had its half-life underestimated during preclin. development because of the difficulty in detecting the drug after the distribution phase has ended.

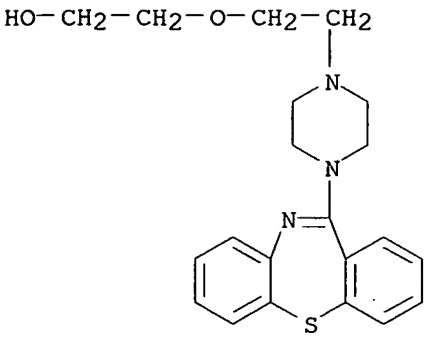
IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(quetiapine fumarate overdose, clin. and pharmacokinetic lessons from extreme conditions)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

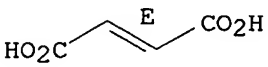
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 48 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:420932 CAPLUS
DOCUMENT NUMBER: 133:48892
TITLE: Conversion of liquid filled gelatin capsules into controlled release systems by multiple coatings
INVENTOR(S): Dong, Liang C.; Wan, Jason; Wong, Patrick S-L.
PATENT ASSIGNEE(S): Alza Corporation, USA
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000035419	A2	20000622	WO 1999-US30341	19991210
WO 2000035419	A3	20001109		
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2354472	AA	20000622	CA 1999-2354472	19991210
EP 1140012	A2	20011010	EP 1999-966463	19991210
EP 1140012	B1	20040303		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
JP 2002532406	T2	20021002	JP 2000-587740	19991210
NZ 512410	A	20030228	NZ 1999-512410	19991210
AU 765909	B2	20031002	AU 2000-21994	19991210
AT 260642	E	20040315	AT 1999-966463	19991210
PT 1140012	T	20040531	PT 1999-966463	19991210
ES 2213404	T3	20040816	ES 1999-966463	19991210
US 2001036472	A1	20011101	US 2001-866036	20010525
US 6419952	B2	20020716		
NO 2001002959	A	20010810	NO 2001-2959	20010615
ZA 2001004928	A	20020618	ZA 2001-4928	20010615
US 2002155154	A1	20021024	US 2002-117359	20020404
PRIORITY APPLN. INFO.:			US 1998-112634P	P 19981217
			US 1999-457803	B1 19991209
			WO 1999-US30341	W 19991210
			US 2001-866036	A1 20010525

AB A dosage form comprises a gelatin capsule formed with a composite wall and containing a liquid, active agent formulation where the wall comprises a barrier layer formed over the external surface of the gelatin capsule, and expandable layer formed over the barrier layer and a semipermeable layer formed over the expandable layer is described. The dosage forms and methods provide for the conversion of standard gelatin, liquid formulation capsules into controlled, release dosage forms that permit the controlled release of the active agent into the environment of use over time.

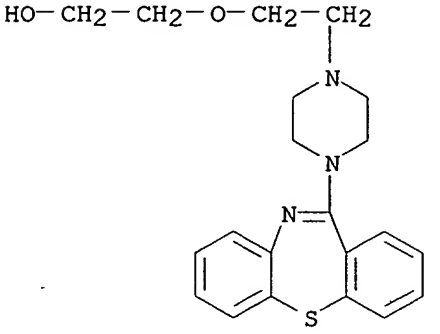
IT **111974-72-2**, Quetiapine fumarate
RL: DEV (Device component use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(conversion of liquid filled gelatin capsules into controlled release systems by multiple coatings)

QUETIAPINE

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

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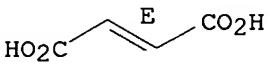


QUETIAPINE

L26 ANSWER 49 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:376345 CAPLUS
DOCUMENT NUMBER: 133:242
TITLE: Pharmacokinetics, tolerability, and clinical effectiveness of quetiapine fumarate: An open-label trial in adolescents with psychotic disorders
AUTHOR(S): McConville, Brian J.; Arvanitis, Lisa A.; Thyrum, Per T.; Yeh, Chiao; Wilkinson, Lisa A.; Chaney, Robert O.; Foster, Keith D.; Sorter, Michael T.; Friedman, Loren M.; Brown, Kerri L.; Heubi, James E.
CORPORATE SOURCE: University of Cincinnati College of Medicine, Cincinnati, OH, 45267-0559, USA
SOURCE: Journal of Clinical Psychiatry (2000), 61(4), 252-260
CODEN: JCLPDE; ISSN: 0160-6689
PUBLISHER: Physicians Postgraduate Press, Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB This is the first investigation of the pharmacokinetics, tolerability, and efficacy of quetiapine fumarate in adolescents with chronic or intermittent psychotic disorders. Ten patients with DSM-IV chronic or intermittent psychotic disorders (ages 12.3 through 15.9 yr) participated in an open-label, rising-dose trial and received oral doses of quetiapine twice daily (b.i.d.), starting at 25 mg b.i.d. and reaching 400 mg b.i.d. by day 20. The trial ended on day 23. Key assessments were pharmacokinetic anal. of plasma quetiapine concns. and neurol., safety, and efficacy evaluations. No statistically significant differences were observed between 100-mg b.i.d. and 400-mg b.i.d. quetiapine regimens for total body clearance, dose-normalized area under the plasma concentration-time curve, or dose-normalized premorning-or postmorning-dose trough plasma values obtained under steady-state conditions after multiple-dose regimens. No unexpected side effects occurred with quetiapine therapy, and no statistically significant changes from baseline were observed for the UKU Side Effect Rating Scale items that were rated. No serious adverse events or clin. important changes in hematol. or clin. chemical variables were reported. The most common adverse events were postural tachycardia and insomnia. Extrapyramidal side effects improved, as evidenced by significant ($p < .05$) decreases from baseline to endpoint in the mean Simpson-Angus Scale total scores and Barnes Akathisia Scale scores. Quetiapine improved pos. and neg. symptoms, as shown by significant ($p < .05$) decreases from baseline to endpoint in the mean Brief Psychiatric Rating Scale total score, the Clin. Global Impressions-Severity of Illness scale, and the Modified Scale for the Assessment of Neg. Symptoms summary score. Quetiapine pharmacokinetics were dose proportional in adolescents and were similar to those previously reported for adults. Quetiapine was well tolerated and effective in the small number of adolescents studied.

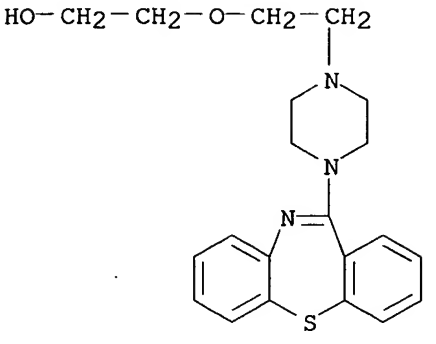
IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(pharmacokinetics, tolerability, and clin. effectiveness of quetiapine fumarate: An open-label trial in adolescents with psychotic disorders)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

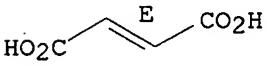
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 40 THERE ARE 40 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 50 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:260000 CAPLUS
DOCUMENT NUMBER: 132:288772
TITLE: Use of metformin to counteract weight gain associated with valproate and other psychotropic medications
INVENTOR(S): Cottingham, Elizabeth Marie
PATENT ASSIGNEE(S): Children's Hospital Research Foundation, USA; Morrison, John Ainslie
SOURCE: PCT Int. Appl., 14 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 2000021522	A1	20000420	WO 1999-US24262	19991015
W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
US 6194466	B1	20010227	US 1999-416330	19991012
AU 9964328	A1	20000501	AU 1999-64328	19991015
EP 1121110	A1	20010808	EP 1999-952021	19991015
EP 1121110	B1	20030820		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
AT 247462	E	20030915	AT 1999-952021	19991015

PRIORITY APPLN. INFO.:

US 1998-104394P	P	19981015
US 1999-416330	A	19991012
WO 1999-US24262	W	19991015

AB A method for minimizing the weight gain side effect associated with psychotropic treatment is disclosed. In the method, Metformin, a biguanide compound, is concurrently administered to a patient taking the psychotropic active. A pharmaceutical composition containing the combination of psychotropic active and Metformin is also disclosed. Psychotropic actives are selected from valproate, Risperdal, Lithobid, Zyprexa and Seroquel.

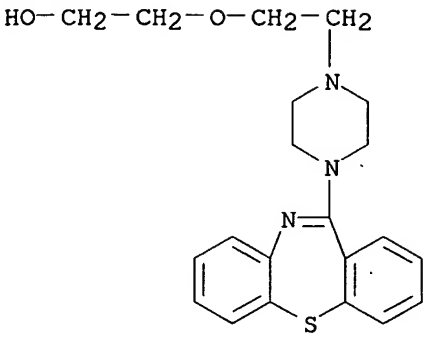
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(metformin to counteract weight gain associated with valproate and other psychotropic medications)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

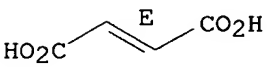
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 8 THERE ARE 8 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 51 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 2000:190381 CAPLUS
DOCUMENT NUMBER: 132:317935
TITLE: A typical antipsychotic effects of quetiapine fumarate in animal models
AUTHOR(S): Guan, Han-Jun; Dai, Jin; Zhu, Xing-Zu
CORPORATE SOURCE: Department of Pharmacology I, Shanghai Institute of Materia Medica, Chinese Academy of Sciences, Shanghai, 200031, Peop. Rep. China
SOURCE: Acta Pharmacologica Sinica (2000), 21(3), 205-210
CODEN: APSCG5
PUBLISHER: Science Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB AIM: To evaluate the effect of quetiapine fumarate in animal models of schizophrenia and its possibility to induce extrapyramidal side effects (EPSE). METHODS: The enhancement of immobility in a forced swimming test of mice induced by repeated treatment with phencyclidine, and amphetamine swimming "normalization" test of mice were used as animal models of neg. and pos. symptoms of schizophrenia, resp. The paw test of rats was used to evaluate the possibility by quetiapine fumarate to induce EPSE. RESULTS: After treatment with phencyclidine (10 mg·kg-1·d-1, s.c., 14 d), the immobility time in the forced swimming test of mice was increased ($P < 0.01$). Quetiapine fumarate (20, 40, and 80 mg·kg-1, ig) and clozapine (10 and 30 mg·kg-1, ig) attenuated the enhanced immobility in the forced swimming test induced by repeated treatment with phencyclidine ($P < 0.01$), whereas haloperidol (0.3 and 1 mg·kg-1, ig) had no effect. In amphetamine swimming "normalization" test, quetiapine fumarate ameliorated the disorder induced by amphetamine in a dose-dependent manner. In paw test, quetiapine fumarate was much less effective in increasing the forelimb retraction time (FRT) than the hindlimb retraction time (HRT). The minimal ED (MED) of HRT (MEDHRT) and FRT (MEDFRT) of quetiapine fumarate was 20 mg·kg-1 and 100 mg·kg-1, resp., and the ratio of MEDFRT to MEDHRT was 5. CONCLUSION: The effects of quetiapine fumarate in these models indicated its clin. effect on schizophrenia with a reduced liability to produce EPSE.

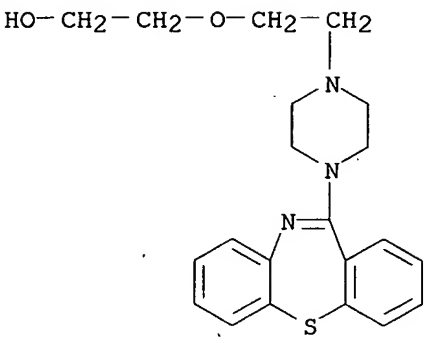
IT **111974-72-2**, Quetiapine fumarate
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(typical antipsychotic effects of quetiapine fumarate in new animal model)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

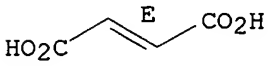
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 52 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:623753 CAPLUS
DOCUMENT NUMBER: 131:346395
TITLE: Inability of Antipsychotics to Antagonize the Cueing Properties of Cocaine in Rats
AUTHOR(S): Van Campenhout, N.; De Haes, P.; Meert, T. F.
CORPORATE SOURCE: Janssen Research Foundation, Pharmacology 3, Beerse, B2340, Belg.
SOURCE: Pharmacology, Biochemistry and Behavior (1999), 64(2), 435-438
CODEN: PBBHAU; ISSN: 0091-3057
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

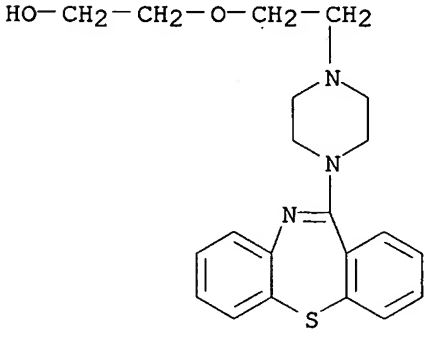
AB In this study the possible antagonistic effects of five different antipsychotics on the discriminative stimulus properties of 10 mg/kg cocaine were evaluated by use of a two-lever food-reinforced drug discrimination procedure in rats. To do so, rats were treated with several doses of haloperidol, risperidone, seroquel, sertindole, and olanzapine, either at 60 or 120 min prior to testing. With all compds. tested, no substantial antagonism of the cocaine cue was observed Only with haloperidol (maximum 60%), risperidone (maximal 20%), and olanzapine (maximal 20%) a partial antagonism without clearcut dose-response was observed Clozapine, seroquel, and sertindole did not influence the discriminative stimulus properties of cocaine. These results indicate that antipsychotics with different pharmacol. profiles are unable to antagonize more than partially the cueing properties of 10 mg/kg cocaine in rats, pointing to the unique underlying stimulus properties of this stimulant.

IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antipsychotics inability to antagonize cocaine cueing properties)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



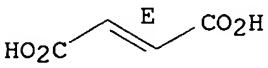
CM 2

CRN 110-17-8

QUETIAPINE

CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 28 THERE ARE 28 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 53 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:608273 CAPLUS
DOCUMENT NUMBER: 132:8660
TITLE: Oxidation Sensitivity May Be a Useful Tool for the Detection of the Hematotoxic Potential of Newly Developed Molecules: Application to Antipsychotic Drugs
AUTHOR(S): Liegeois, Jean-Francois; Bruhwyler, Jacques; Petit, Christine; Damas, Jacques; Delarge, Jacques; Geczy, Joseph; Kauffmann, Jean-Michel; Lamy, Maurice; Meltzer, Herbert; Mouithys-Mickalad, Ange
CORPORATE SOURCE: Laboratory of Medicinal Chemistry, University of Liege, Liege, B-4000, Belg.
SOURCE: Archives of Biochemistry and Biophysics (1999), 370(1), 126-137
CODEN: ABBIA4; ISSN: 0003-9861
PUBLISHER: Academic Press
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Some antipsychotic agents have been found to produce agranulocytosis and aplastic anemia. The oxidation phenomena and/or the formation of free radicals has been suggested to be causally related to various hematol. disorders, e.g., agranulocytosis. Using five exptl. conditions, the authors tested the oxidative potential of compds. with and without a history of hematol. side effects, e.g., agranulocytosis and aplastic anemia. A statistical anal. was undertaken for each exptl. condition and a multivariate anal. combining all results was performed. Two peroxidase-induced free radical models did not successfully discriminate between drugs with and without a history of causing hematol. problems (<70%). The lipid peroxidn. system provided even less satisfactory discrimination, with only 56.25% correct classification. However, an 87.5% correct classification was obtained when using the oxidation potentials of these drugs determined at pH 4.7 and at pH 7.4. A multivariate anal. taking into account the five variables provided 87.5% success in classification. The two clusters were better discriminated in terms of a "distance coefficient". In a second anal., the putative antipsychotic pyridobenzodiazepine analogs (JL5, JL8, JL18, and JL25) were classified in the cluster of toxic compds., while the oxa- and thiazepine analogs (JL2, JL3, and JL13) were classified as nontoxic compds. A few metabolites of clozapine and fluperlapine were classified in the toxic compound group. The procedure described herein is, to the authors knowledge, the first which classifies mols. of different structures as well as different pharmacol. profiles according to their hematotoxic potential. Such a procedure could be used to predict drug-induced hematol. side effects. (c) 1999 Academic Press.

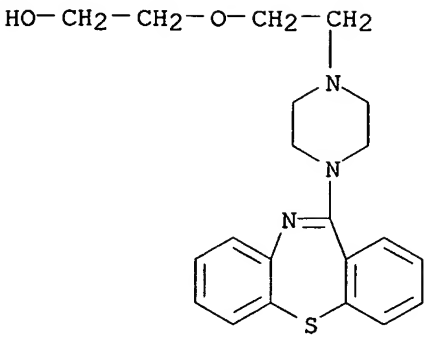
IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); ANT (Analyte); PRP (Properties); ANST (Analytical study); BIOL (Biological study)
(oxidation sensitivity may be a useful tool for detection of hematotoxic potential of newly developed mols. and application to antipsychotic drugs)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

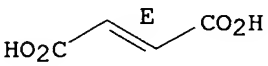
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 77 THERE ARE 77 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 54 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:607974 CAPLUS
DOCUMENT NUMBER: 132:117441
TITLE: Involvement of serotonin 2A receptors in phencyclidine-induced disruption of prepulse inhibition of the acoustic startle in rats
AUTHOR(S): Yamada, S.; Harano, M.; Annoh, N.; Nakamura, K.; Tanaka, M.
CORPORATE SOURCE: Institute of Brain Diseases, Kurume University School of Medicine, Kurume, Japan
SOURCE: Biological Psychiatry (1999), 46(6), 832-838
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The disruption of prepulse inhibition of acoustic startle (PPI) is an animal model for some aspects of schizophrenia. Phencyclidine causes psychotomimetic symptoms in human and disrupts PPI in animals, however, the mechanism underlying this disruption remains unclear. The present experiment tested the hypothesis that serotonin 2A receptor blocking property of drugs reverses the phencyclidine-induced PPI disruption. The ED50 value of spiperone, haloperidol, chlorpromazine, clozapine, risperidone, olanzapine, seroquel, pipamperone, mianserin, or desipramine to reverse the phencyclidine- or apomorphine-induced PPI disruption in rats was determined Then the correlation between the ED50 value and the affinity for the serotonin 2A, 2C, dopamine D2, or α-1 receptor of each drug was examined The ED50 value of the drugs to reverse the phencyclidine-induced PPI disruption was correlated with the affinity for the serotonin 2A receptor, but not for the dopamine D2, serotonin 2C, or α-1 receptor of each drug. In contrast, the ED50 value of the drugs to reverse the apomorphine-induced PPI disruption was correlated with the affinity for the dopamine D2 receptor, but not for the serotonin 2A receptor. An activation of serotonin 2A receptors would mediate the phencyclidine-induced PPI disruption.

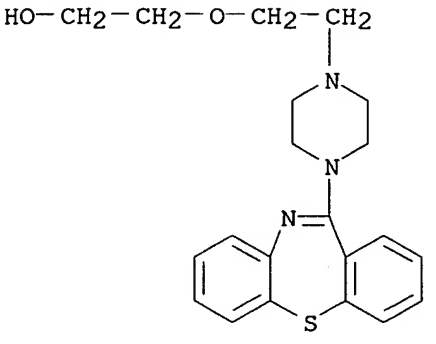
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effect of neuroleptics on apomorphine- or phencyclidine-induced disruption of prepulse inhibition)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

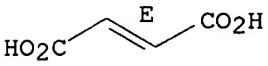
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 55 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:507447 CAPLUS
DOCUMENT NUMBER: 132:59039
TITLE: Regulation of ionotropic glutamate receptors in the rat brain in response to the atypical antipsychotic seroquel (quetiapine fumarate)
AUTHOR(S): Tascedda, F.; Lovati, E.; Blom, J. M. C.; Muzzioli, P.; Brunello, N.; Racagni, G.; Riva, M. A.
CORPORATE SOURCE: Center for Neuropharmacology, Institute of Pharmacological Sciences, University of Milan, Milan, 20133, Italy
SOURCE: Neuropsychopharmacology (1999), 21(2), 211-217
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The interplay between dopamine and glutamate appears to be relevant in the etiopathol. of schizophrenia. Although currently used antipsychotics do not interact with glutamatergic receptors, previous results have demonstrated that the expression profile of ionotropic glutamate receptors can be regulated by drugs such as haloperidol or clozapine. In the present investigation, the mRNA levels for NMDA and AMPA receptor subunits were measured after chronic treatment with the novel antipsychotic agent Seroquel (quetiapine fumarate, quetiapine) as compared to haloperidol and clozapine. Similarly to the prototype atypical clozapine, quetiapine reduced the mRNA expression for NR-1 and NR-2C, two NMDA forming subunits, in the nucleus accumbens. Furthermore, quetiapine, but not haloperidol or clozapine, increased the hippocampal expression for the AMPA subunits GluR-B and GluR-C. The differences between classical and atypical antipsychotics, as well as among the novel agents, might be relevant for specific aspects of their therapeutic activity and could provide valuable information for the role of glutamate in specific symptoms of schizophrenia.

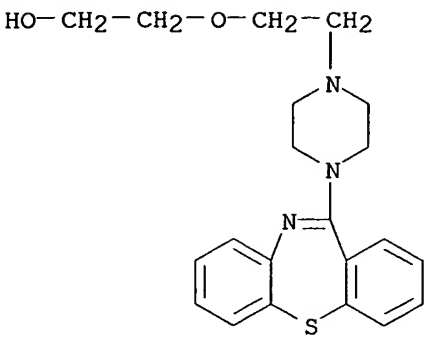
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(NMDA and AMPA receptor subunits response to treatment with antipsychotics)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

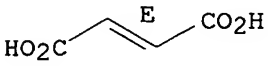
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 36 THERE ARE 36 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 56 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:390064 CAPLUS
DOCUMENT NUMBER: 131:39094
TITLE: Quetiapine fumarate (Seroquel): a new atypical antipsychotic
AUTHOR(S): Goldstein, Jeffrey M.
CORPORATE SOURCE: Clinical Medicine Group, Zeneca Pharmaceuticals, Wilmington, DE, USA
SOURCE: Drugs of Today (1999), 35(3), 193-210
CODEN: MDACAP; ISSN: 0025-7656
PUBLISHER: Prous Science
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with 76 refs. The goal of antipsychotic drug development efforts over the past 10 yr has been to develop agents with increased efficacy and safety and fewer of the side effects commonly associated with the older antipsychotic medications. The newer agents, often called atypical antipsychotics, are effective in treating both the pos. and neg. symptoms of schizophrenia and are associated with fewer neurol.- and endocrine-related side effects than the older agents. As a result, patients are likely to remain on therapy longer, preventing relapses and costly hospitalizations. Quetiapine fumarate (Seroquel), is the most recently introduced atypical antipsychotic and is indicated for the management of the manifestations of psychotic disorders and schizophrenia. Quetiapine, like clozapine (the archetypal atypical antipsychotic), interacts with a broad range of neurotransmitter receptors and has a higher affinity for serotonin (5-HT2A) receptors than for dopamine (D2) receptors in the brain. Further, quetiapine's pharmacol. effects appear selective for the mesolimbic and mesocortical dopamine systems, which are believed to be the areas of the brain responsible for the therapeutic effects of antipsychotics. In contrast to most standard antipsychotics and some atypical antipsychotics, quetiapine's effects on the nigrostriatal dopamine system, which is responsible for the extrapyramidal (or motor) side effects, are minimal. Quetiapine also has minimal activity on dopamine receptors in the tuberoinfundibular dopamine system, thereby avoiding the problem of hyperprolactinemia, common with the standard antipsychotics and some atypical antipsychotics. Because of these properties, quetiapine is an effective antipsychotic agent with a relatively benign side effect profile. Several large, placebo- and active-controlled, multicenter trials have shown quetiapine to be effective against both pos. (e.g., hallucinations, delusions) and neg. symptoms (e.g., emotional withdrawal, apathy) and to have benefits in reducing hostility, aggression and affective symptoms. Patients on long-term treatment report high compliance, good satisfaction, increased ability to function and improvements consistent with a better quality of life. Because of quetiapine's excellent tolerability profile, its use is particularly appropriate in patients especially sensitive to adverse effects, e.g., elderly patients with psychotic symptoms and other neurol. disorders such as Parkinson's and Alzheimer's disease.

IT **111974-72-2**, Quetiapine fumarate
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(quetiapine fumarate pharmacol. as an atypical antipsychotic in humans)

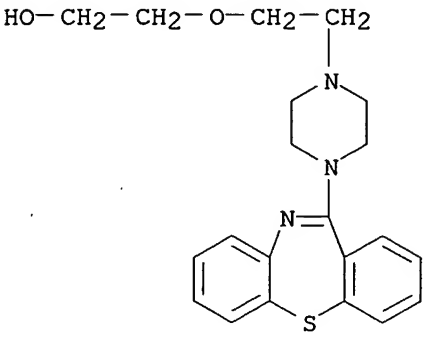
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7

QUETIAPINE

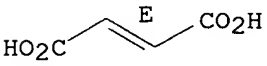
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 76 THERE ARE 76 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 57 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:297269 CAPLUS
DOCUMENT NUMBER: 130:332902
TITLE: Treatment of schizophrenia with AMPAkines and neuroleptics
INVENTOR(S): Johnson, Steven A.; Rogers, Gary A.; Lynch, Gary S.
PATENT ASSIGNEE(S): Cortex Pharmaceuticals, Inc., USA; The Regents of the University of California
SOURCE: PCT Int. Appl., 59 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9921422	A1	19990506	WO 1998-US22707	19981026
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, GM, KE, LS, MW, SD, SZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG				
CA 2306817	AA	19990506	CA 1998-2306817	19981026
AU 9913658	A1	19990517	AU 1999-13658	19981026
AU 745641	B2	20020328		
EP 1026950	A1	20000816	EP 1998-957382	19981026
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
BR 9814106	A	20001003	BR 1998-14106	19981026
US 6166008	A	20001226	US 1998-179341	19981026
JP 2001520978	T2	20011106	JP 2000-517599	19981026
PRIORITY APPLN. INFO.:			US 1997-63627P P	19971027
			WO 1998-US22707 W	19981026

OTHER SOURCE(S): MARPAT 130:332902

AB The invention relates to treatment of schizophrenia and related psychotic disorders, including enhancement of receptor functioning in synapses in brain networks responsible for higher order behaviors. In a particular aspect, the invention relates to methods for the use of AMPA receptor up-modulators in conjunction with antipsychotics for the treatment of schizophrenia. Kits containing the compns. in appropriate form for administration are also provided. A representative AMPAkine (CX516) synergistically enhanced clozapine antagonism of methamphetamine-induced rearing activity.

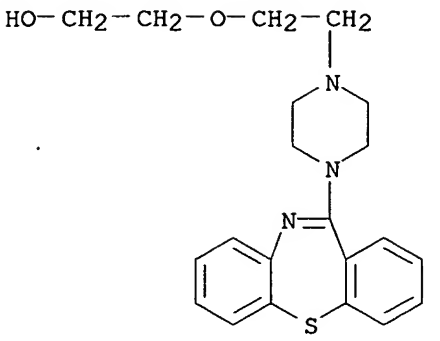
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(AMPAkines and antipsychotic agents for treatment of schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

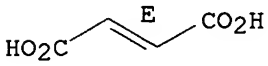
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 2 THERE ARE 2 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 58 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1999:99734 CAPLUS
DOCUMENT NUMBER: 130:291466
TITLE: Atypical neuroleptics enhance histamine turnover in brain via 5-hydroxytryptamine2A receptor blockade
AUTHOR(S): Morisset, S.; Sahm, U. G.; Traiffort, E.; Tardivel-Lacombe, J.; Arrang, J. M.; Schwartz, J.-C.
CORPORATE SOURCE: Unite de Neurobiologie et Pharmacologie Moleculaire, Institut National de la Sante et de la Recherche Medicale, Paris, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1999), 288(2), 590-596
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: American Society for Pharmacology and Experimental Therapeutics
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clozapine and olanzapine behave as weak H3-receptor antagonists in vitro, with Ki values around 1 and 50 μM, resp. Despite these modest apparent affinities, both compds., when given orally to mice, nearly doubled steady-state levels of the histamine metabolite tele-methylhistamine in brain, with ED50 values as low as 1 and 3 mg/kg, resp., an effect comparable to those of potent H3-receptor antagonists. This effect corresponded to an enhancement of histamine turnover rate from 45 to 73 ng/g/h, in the case of olanzapine. Other antipsychotics displaying high 5-hydroxytryptamine (5-HT)2A receptor antagonist potency, i.e., risperidone, thioridazine, seroquel, and iloperidone, also markedly enhanced tele-methylhistamine levels. This effect was: (1) additive with that of a pure H3-receptor antagonist, ciproxifan, (2) mimicked by a 5-HT2A receptor antagonist, ketanserin, (3) reversed by a 5-HT2A receptor agonist, DOI, (4) not shared by antipsychotics with low affinity for the 5-HT2A receptor, i.e., haloperidol, sulpiride, raclopride, or remoxipride which, on the contrary, tended to reduce tele-methylhistamine levels. It is concluded that in contrast to "typical" antipsychotics, "atypical" antipsychotics stimulate neuronal histamine activity via blockade of the 5-HT2A receptor in vivo. This effect does not appear to account for their reduced extrapyramidal side-effects but may underlie their procognitive properties.

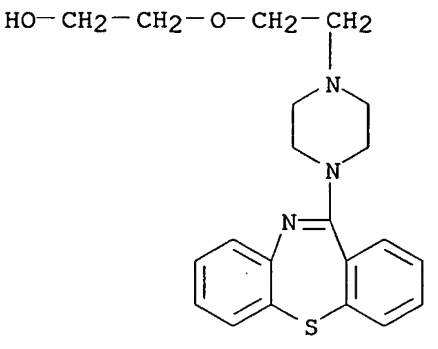
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(atypical neuroleptics enhancement of histamine turnover in brain via 5-hydroxytryptamine2A receptor blockade)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

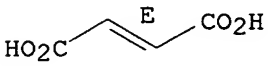
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 41 THERE ARE 41 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

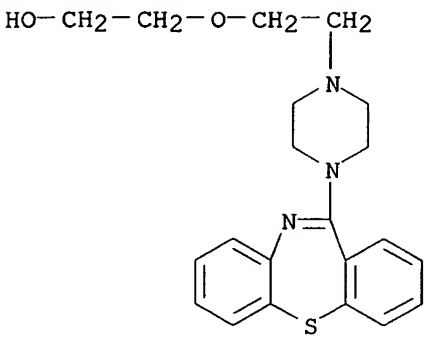
QUETIAPINE

L26 ANSWER 59 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:797716 CAPLUS
DOCUMENT NUMBER: 130:148606
TITLE: Seroquel, clozapine and chlorpromazine restore sensorimotor gating in ketamine-treated rats
AUTHOR(S): Swerdlow, Neal R.; Bakshi, Vaishali; Waikar, Manoj; Taaid, Navid; Geyer, Mark A.
CORPORATE SOURCE: Department of Psychiatry and Neuroscience Program, School of Medicine, University of California, San Diego, La Jolla, CA, 92093-0804, USA
SOURCE: Psychopharmacology (Berlin) (1998), 140(1), 75-80
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Sensorimotor gating of the startle reflex (as measured by prepulse inhibition (PPI)) is impaired in schizophrenia patients and in rats treated with either dopamine (DA) agonists or with N-methyl-D-aspartate (NMDA) antagonists. While both typical and atypical antipsychotics restore PPI in DA agonist-treated rats, studies thus far have demonstrated that only atypical antipsychotics restore PPI in rats treated with NMDA antagonists. This model for predicting atypical antipsychotic properties has been studied extensively in rats, and there is interest in moving these studies into humans, where the NMDA antagonist ketamine is also reported to reduce PPI. This model was used to study the effects of high- and low-potency typical antipsychotics (haloperidol and chlorpromazine), the atypical antipsychotic clozapine, and the putative atypical antipsychotic Seroquel on ketamine-disrupted PPI in rats, across a range of ketamine doses that produced submaximal, as well as maximal, disruptions of PPI. Ketamine dose-dependently reduced PPI, and this effect was opposed by Seroquel, clozapine and chlorpromazine, but not haloperidol. The effects of chlorpromazine on ketamine-disrupted PPI demonstrate that the ability of antipsychotics to restore PPI in NMDA antagonist-treated rats is not specific to clin. atypical antipsychotics. Receptor properties shared by Seroquel, clozapine and chlorpromazine, but not haloperidol, may implicate critical substrates in the NMDA antagonist-induced disruption of PPI.
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(sensorimotor gating of startle reflex in ketamine-treated rats restoration by)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

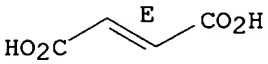
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



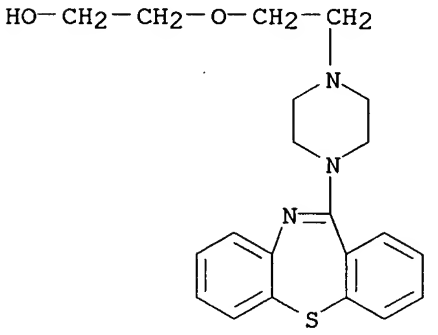
REFERENCE COUNT: 21 THERE ARE 21 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 60 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:389427 CAPLUS
DOCUMENT NUMBER: 129:36021
TITLE: ICI 204,636 (quetiapine). A novel antipsychotic agent
AUTHOR(S): Wakao, Harumitsu; Izushi, Koji; Yamashita, Sueo
CORPORATE SOURCE: Pharm. Med. Res. Dep., Zeneca K. K., Osaka, 531-0076, Japan
SOURCE: No no Kagaku (1998), 20(6), 677-681
CODEN: NNOKFZ; ISSN: 1343-4144
PUBLISHER: Seiwa Shoten
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese
AB A review with 12 refs., on the structure, pharmacokinetics, and clin. efficacy of antipsychotic ICI 204,636 (quetiapine).
IT **111974-72-2**, ICI 204636
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); PRP (Properties); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(ICI 204,636, a novel antipsychotic agent)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

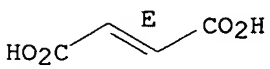
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 61 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:235094 CAPLUS
DOCUMENT NUMBER: 128:303969
TITLE: Reversal of isolation rearing-induced deficits in prepulse inhibition by Seroquel and olanzapine
AUTHOR(S): Bakshi, Vaishali P.; Swerdlow, Neal R.; Braff, David L.; Geyer, Mark A.
CORPORATE SOURCE: Department of Neurosciences, University of California at San Diego, La Jolla, CA, 92093-0804, USA
SOURCE: Biological Psychiatry (1998), 43(6), 436-445
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier Science Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

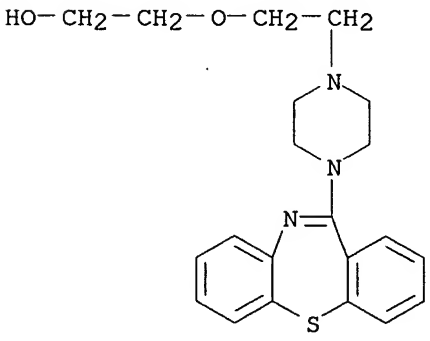
AB Prepulse inhibition (PPI) of startle provides an operational measure of sensorimotor gating in which a weak stimulus presented prior to a startling stimulus reduces the startle response. PPI deficits observed in schizophrenia patients can be modeled in rats by individual housing from weaning until adulthood. Deficits in PPI produced by isolation rearing can be reversed by antipsychotics. We evaluated the ability of Seroquel and olanzapine to reverse the isolation-induced disruption of PPI. Rats housed for 8 wk singly or in groups of 3 were tested every 2 wk after either Seroquel (0, 5.0 mg/kg) or olanzapine (0, 2.5, 5.0 mg/kg). Startle was elicited by 120-dB pulses presented either with or without prepulses (3, 6, or 12 dB above a 65-dB background). Isolation rearing repeatedly disrupted PPI and sometimes increased startle reactivity. Seroquel reversed these deficits without affecting PPI in socially reared controls. Olanzapine (2.5 mg/kg) reversed the isolation rearing-induced PPI deficit and tended to increase basal PPI levels. Both antipsychotics antagonized the isolation rearing-induced increase in startle reactivity. Isolation rearing produces deficits in sensorimotor gating in rats that are reversible by atypical antipsychotics, and may therefore aid in identifying new treatments for schizophrenia.

IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(reversal of isolation rearing-induced deficits in prepulse inhibition by Seroquel and olanzapine)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

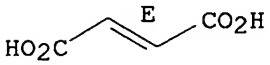


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 62 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1998:168555 CAPLUS
DOCUMENT NUMBER: 128:290115
TITLE: Comparative characterization of the discriminative stimulus properties of clozapine and other antipsychotics in rats
AUTHOR(S): Goudie, Andrew; Taylor, Anita
CORPORATE SOURCE: Psychology Department, Liverpool University, Liverpool, L69 7ZA, UK
SOURCE: Psychopharmacology (Berlin) (1998), 135(4), 392-400
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer-Verlag
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The discriminative stimulus properties of the prototypical atypical neuroleptic clozapine (5 mg/kg, i.p.) were characterized in rats using a fixed ratio assay. Clozapine induced full dose-related generalization in the absence of response suppression. Amphetamine and pentylenetetrazol failed to generalize at doses known to be discriminable, showing a degree of specificity for the clozapine cue. The typical neuroleptics haloperidol and loxapine induced minimal (20%) generalization at doses with marked behavioral effects; thus clozapine discrimination dissocs. clozapine from typical neuroleptics. Atypical neuroleptics which are not clozapine congeners produced weak partial generalization when tested up to the highest doses that could be studied. The maximal levels of generalization induced by these agents were: amisulpiride 28%, risperidone 40% and sertindole 50%. Clozapine congeners typically caused more generalization, the novel pyridobenzoxapine JL13 inducing 70% maximal generalization. Most generalization (83%) was seen with the clozapine congener seroquel, although in contrast to clozapine, it only generalized at doses with marked effects on responding, so that no drug mimicked clozapine fully. Surprisingly, the clozapine congener olanzapine only induced a maximal level of 38% generalization. This apparently anomalous finding is attributed to an inability to test high doses of the drug due to its rate-suppressant actions. The clozapine cue can be used to rank atypical neuroleptics in terms of their similarity to clozapine in vivo. The clozapine cue is probably a compound cue, since only agents showing "polyvalent" receptor pharmacol. induced substantial generalization.

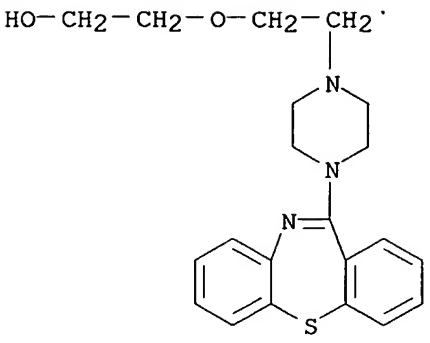
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(comparative characterization of the discriminative stimulus properties of clozapine and other antipsychotics in rats)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

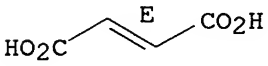
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 50 THERE ARE 50 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 63 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:803816 CAPLUS
DOCUMENT NUMBER: 128:66491
TITLE: Sustained-release pharmaceuticals containing dibenzothiazepine
INVENTOR(S): Parikh, Bhavnish Vinod; Timko, Robert Joseph; Addicks, William Joseph
PATENT ASSIGNEE(S): Zeneca Limited, UK
SOURCE: PCT Int. Appl., 36 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9745124	A1	19971204	WO 1997-GB1432	19970527
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2251944	AA	19971204	CA 1997-2251944	19970527
AU 9729675	A1	19980105	AU 1997-29675	19970527
AU 727219	B2	20001207		
EP 907364	A1	19990414	EP 1997-924103	19970527
EP 907364	B1	20020814		
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO				
CN 1219879	A	19990616	CN 1997-194961	19970527
BR 9709271	A	19990810	BR 1997-9271	19970527
NZ 332198	A	20000526	NZ 1997-332198	19970527
JP 2000511170	T2	20000829	JP 1997-541846	19970527
IL 127222	A1	20010319	IL 1997-127222	19970527
AT 222105	E	20020815	AT 1997-924103	19970527
PT 907364	T	20021231	PT 1997-924103	19970527
ES 2182079	T3	20030301	ES 1997-924103	19970527
RU 2201754	C2	20030410	RU 1998-123601	19970527
CZ 293760	B6	20040714	CZ 1998-3880	19970527
SK 284131	B6	20040908	SK 1998-1639	19970527
US 5948437	A	19990907	US 1997-864306	19970528
HR 970299	B1	20011231	HR 1997-970299	19970528
ZA 9704735	A	19971201	ZA 1997-4735	19970529
TW 550076	B	20030901	TW 1997-86107689	19970604
KR 2000011013	A	20000225	KR 1998-709163	19981113
NO 9805539	A	19981127	NO 1998-5539	19981127

PRIORITY APPLN. INFO.:	GB 1996-11328	A	19960531
	US 1996-18816P	P	19960531
	WO 1997-GB1432	W	19970527

AB The invention relates to sustained release formulations comprising 11-[4-[2-(2-hydroxyethoxy)ethyl]-1-piperazinyl]dibenzo[b,f][1,4]thiazepine (I) or a salt to methods of treating psychotic states and hyperactivity utilizing the sustained-release formulations. Thus, tablets contained I hemifumarate 460.51, lactose 152.62, microcryst. cellulose 50.87, Methocel E50LV 120.00, and magnesium stearate 16.00 mg/tablet and water qs.

IT **111974-72-2**
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)

QUETIAPINE

(sustained-release pharmaceuticals containing dibenzothiazepine)

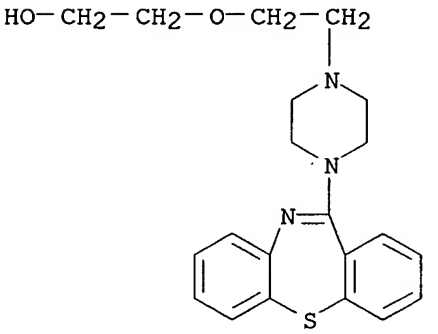
RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7

CMF C21 H25 N3 O2 S

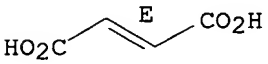


CM 2

CRN 110-17-8

CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 64 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:749516 CAPLUS
DOCUMENT NUMBER: 128:70673
TITLE: Phencyclidine-induced deficits in prepulse inhibition of startle are blocked by prazosin, an alpha-1 noradrenergic antagonist
AUTHOR(S): Bakshi, Vaishali P.; Geyer, Mark A.
CORPORATE SOURCE: Department of Neurosciences and Psychiatry, University of California at San Diego, La Jolla, CA, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 283(2), 666-674
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Prepulse inhibition (PPI) is a form of plasticity of the startle response in which presentation of a weak stimulus immediately before an intense starting stimulus reduces the resultant startle response. Deficits in PPI, an operational measure of sensorimotor gating, are observed in schizophrenia patients and can be modeled in rats by the psychotogen phencyclidine (PCP). PCP-induced deficits in PPI in rats are resistant to dopamine and serotonin antagonists but can be antagonized by antipsychotics such as clozapine, olanzapine and Seroquel. These latter antipsychotics have antagonistic actions at several receptors, including alpha-1 and alpha-2 adrenergic, M1 muscarinic and γ-aminobutyric acid (GABA)-A receptors. Although the direct actions of PCP are thought to be mediated by noncompetitive antagonism of N-methyl-D-aspartate sites, PCP thereby indirectly activates multiple neurotransmitter systems, including those affected by the aforementioned antipsychotics. The present studies examined the possibility that an antagonist action at a particular receptor subtype might be responsible for the interaction between PCP and the clozapine-like antipsychotics by testing whether a selective antagonist at alpha-1, alpha-2, M1 or GABA-A receptors would prevent the PCP-induced deficit in PPI in rats. Animals were pretreated with either the alpha-1 antagonist prazosin (0, 0.5, 1.0 or 2.5 mg/kg), the alpha-2 antagonist RX821002 (0, 0.2 or 0.4 mg/kg), the M1 muscarinic antagonist pirenzepine (0, 10 or 30 mg/kg) or the GABA-A antagonist pitrazepin (0, 1.0 or 3.0 mg/kg) and then treated with either saline or PCP (1.5 mg/kg). Because prazosin was effective in blocking the effects of PCP, an addnl. experiment tested the possibility that prazosin (0, 1.0 or 2.5 mg/kg) would block the PPI deficits produced by the dopamine agonist apomorphine (0 or 0.5 mg/kg). After drug administration, animals were tested in startle chambers PCP was found repeatedly to decrease PPI. Prazosin (1.0 and 2.5 mg/kg) blocked this deficit in two sep. expts. but did not increase base-line PPI levels. The effects on PPI were dissociable from changes in startle reactivity. Furthermore, prazosin did not antagonize apomorphine-induced disruptions of PPI, which suggests that the antagonism of the PCP effect was not simply due to a generalized improvement of deficient PPI. The antagonists for alpha-2, for M1 and for GABA-A receptors had no effect on base-line PPI or on PCP-induced disruptions in PPI. These findings indicate that the PPI-disruptive effect of PCP may be mediated in part by alpha-1 adrenergic receptors and that antagonism of alpha-1 receptors may play a major role in mediating the blockade of PCP-induced deficits in PPI by certain antipsychotics.

IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(mechanism of phencyclidine-induced deficits in prepulse inhibition of startle and effects of antipsychotics)

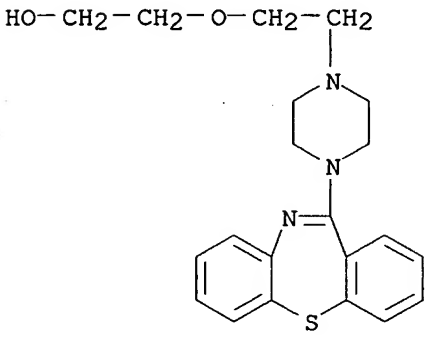
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-,

QUETIAPINE

(2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

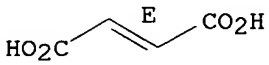
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 74 THERE ARE 74 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 65 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:712225 CAPLUS
DOCUMENT NUMBER: 128:18607
TITLE: Binding of typical and atypical antipsychotic drugs to multiple neurotransmitter receptors
AUTHOR(S): Roth, Bryan L.; Meltzer, H. Y.; Khan, Naseem
CORPORATE SOURCE: Deps. Psychiatry, Neuroscis.. Biochem. Case Western Res. Univ. Med. Sch., Cleveland, OH, 44106, USA
SOURCE: Advances in Pharmacology (San Diego) (1998), 42(Catecholamines), 482-485
CODEN: ADPHEL; ISSN: 1054-3589
PUBLISHER: Academic
DOCUMENT TYPE: Journal
LANGUAGE: English

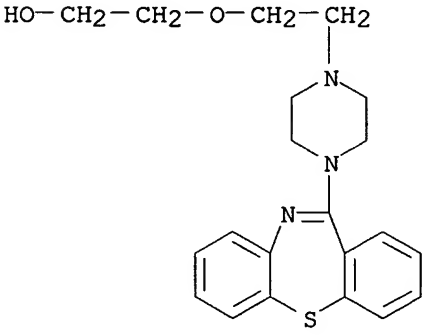
AB The authors investigated the spectrum of drug binding of clin. available atypical antipsychotic drugs to multiple dopamine and 5-HT receptors and compared their binding spectrums with typical antipsychotic drugs. It appeared that atypical antipsychotic drugs are, in general, characterized by low D2 dopamine receptor affinity and relatively high affinities for various 5-HT receptors (5HT2A, 5HT2C, 5HT6, 5HT7). The results suggest that since atypical antipsychotic drugs have relatively high affinity for a number of different receptors, ascribing their unique effects to any one receptor is likely to be unproductive.

IT **111974-72-2**, Seroquel
RL: BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(binding of typical and atypical antipsychotic drugs to multiple dopamine and 5-HT receptors)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

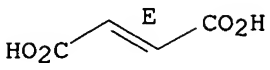


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



REFERENCE COUNT: 7 THERE ARE 7 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 66 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:702961 CAPLUS
DOCUMENT NUMBER: 127:341727
TITLE: ICI 204,636, an atypical antipsychotic: efficacy and safety in a multicenter, placebo-controlled trial in patients with schizophrenia
AUTHOR(S): Borison, Ricahrd L.; Arvanitis, Lisa A.; Miller, Barbara G.; Alphs, Larry D.; Carman, John S.; Diamond, Bruce; Gewirtz, George; Hamner, Mark B.; Hirshfield, Robert; McEvoy, Joseph P.; Mukherjee, Sukdeb; Nasrallah, Henry A.; Oxenkrug, Gregory; Ryan, William; Smith, Nathan; Tamminga, Carol
CORPORATE SOURCE: Augusta Veterans Administration Med. Cent., Augusta, GA, 30910, USA
SOURCE: Journal of Clinical Psychopharmacology (1996), 16(2), 158-169
CODEN: JCPYDR; ISSN: 0271-0749
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB ICI 204,636 is a new, potentially atypical antipsychotic. In early phase II trials, the antipsychotic was well tolerated and results suggested efficacy in the treatment of the pos. and neg. symptoms of schizophrenia. The efficacy and safety of ICO 204,636 were evaluated on a larger scale in a 6-wk, multicenter, double-blind trial. Hospitalized patients who met DSM-III-R criteria for chronic or subchronic schizophrenia with acute exacerbation, as well as other criteria, were randomized to ICI 204,636 (75 to 750 mg daily) (N = 54) or placebo (N = 55). Patients were assessed weekly by use of the Brief Psychiatric Rating Scale (BPRS), Scale for the Assessment of Neg. Symptoms (SANS), and Clin. Global Impression Scale (CGI) for efficacy and the Simpson Scale and Abnormal Involuntary Movement Scale for extrapyramidal side effects (EPS). Significant differences ($p \leq 0.05$) between treatment groups, which favored ICI 204,636 were identified throughout the trial. Endpoint differences were significant (by anal. of covariance) for BPRS factor IV (activation) and SANS scores and were marginally significant for total BPRS, BPRS factor III (thought disturbance), BPRS pos.-symptom cluster, and CGI Severity of Illness item scores ($p = 0.07$, 0.09, 0.06, and 0.09, resp.). ICI 204,636 was well tolerated, although it was associated with mild transient increases in alanine aminotransferase and a higher incidence of somnolence and anticholinergic effects compared with placebo. In the dose range studied, treatment with ICI 204,636 did not induce EPS as determined by anal. of Simpson Scale total scores and lack of treatment-emergent acute dystonic reactions. Furthermore, ICI 204,636 did not produce sustained levels of prolactin; the mean change from baseline at endpoint (-7.2 μg/L) was comparable ($p = 0.44$) to that for placebo (-8.2 μg/L). These findings distinguish ICI 204,636 from standard antipsychotics and confirm preclin. predictions that ICI 204,636 is an atypical antipsychotic.

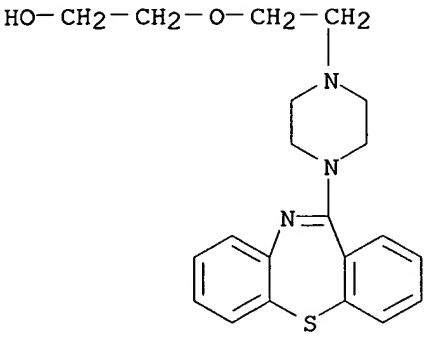
IT **111974-72-2**, ICI 204636
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(ICI 204,636 in treatment of schizophrenia in humans)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

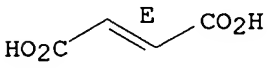
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 22 THERE ARE 22 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 67 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:650272 CAPLUS
DOCUMENT NUMBER: 127:298753
TITLE: Method for treating pain with an atypical antipsychotic compound
INVENTOR(S): Helton, David R.; Shannon, Haarlan E.; Womer, Daniel E.
PATENT ASSIGNEE(S): Eli Lilly and Company, USA
SOURCE: PCT Int. Appl., 24 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9735584	A1	19971002	WO 1997-US4699	19970324
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
CA 2250042	AA	19971002	CA 1997-2250042	19970324
AU 9725872	A1	19971017	AU 1997-25872	19970324
EP 906104	A1	19990407	EP 1997-917594	19970324
R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, NL, SE, PT, IE, FI				
JP 2000507544	T2	20000620	JP 1997-534520	19970324
US 6444665	B1	20020903	US 2000-498047	20000204
US 2003013689	A1	20030116	US 2002-224224	20020815

PRIORITY APPLN. INFO.:	US 1996-14152P	P 19960325
	US 1997-823458	B1 19970324
	WO 1997-US4699	W 19970324
	US 2000-498047	A3 20000204

AB The present invention provides a method for treating pain using an atypical antipsychotic compound Tablet formulations were given for compds. such as risperidone.

IT **111974-72-2**, Seroquel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(treating pain with an atypical antipsychotic compound)

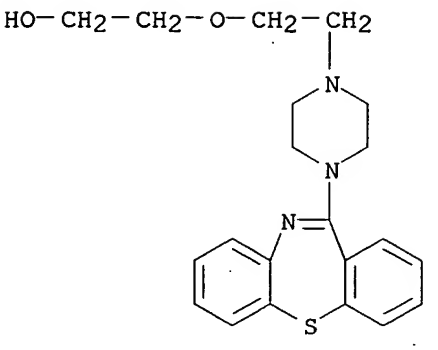
RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

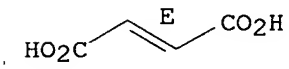
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 68 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:594839 CAPLUS
DOCUMENT NUMBER: 127:257606
TITLE: Assessment of the responsiveness of individuals to modulators of the 5-HT2 receptors, especially the 5-HT2A receptor, by detection of receptor allele DNA
INVENTOR(S): Kerwin, Robert; Collier, David; Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Smithkline Beecham PLC, UK; Kerwin, Robert; Collier, David; Roberts, Gareth Wyn
SOURCE: PCT Int. Appl., 18 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9732037	A1	19970904	WO 1997-EP993	19970226
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, GH, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, YU, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: GH, KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9718789	A1	19970916	AU 1997-18789	19970226
JP 2000506009	T2	20000523	JP 1997-530621	19970226
ZA 9701775	A	19971128	ZA 1997-1775	19970228
PRIORITY APPLN. INFO.:			GB 1996-4465 A	19960301
			WO 1997-EP993 W	19970226

AB A method is disclosed for use in assessing, in a subject suffering from a condition which may be treated with a 5-HT2 modulator, the likelihood whether the subject will be responsive or nonresponsive to treatment with a 5-HT2 modulator. The method comprises detecting the presence or absence of DNA encoding the Tyr452 and/or His452 alleles of the 5-HT2A gene in a biol. sample obtained from the subject. Genotyping for His452Tyr polymorphism was carried out using blood samples from individuals diagnosed as suffering from schizophrenia and being treated with clozapine. The individuals were also sep. assessed for responsiveness to clozapine treatment.

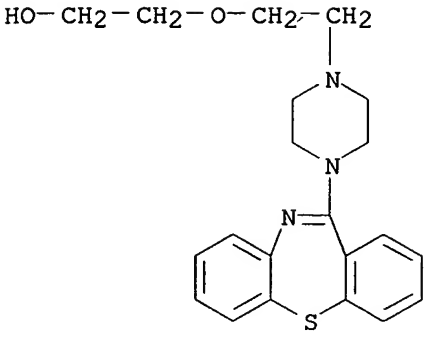
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(5-HT2 receptor modulator responsiveness assessment by detection of receptor allele DNA)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

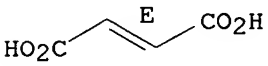
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 69 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:551669 CAPLUS
DOCUMENT NUMBER: 127:185780
TITLE: Multiple fixed doses of "Seroquel" (quetiapine) in patients with acute exacerbation of schizophrenia: a comparison with haloperidol and placebo
AUTHOR(S): Arvanitis, Lisa A.; Miller, Barbara G.; The Seroquel Trial Thirteen Study Group
CORPORATE SOURCE: Zeneca Pharmaceuticals, Wilmington, DE, 19850, USA
SOURCE: Biological Psychiatry (1997), 42(4), 233-246
CODEN: BIPCBF; ISSN: 0006-3223
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Five fixed doses of the atypical antipsychotic "Seroquel" (quetiapine) were evaluated to delineate a dose-response relationship, as measured by changes from baseline in Brief Psychiatric Rating Scale (BPRS), Clin. Global Impression (CGI), and Modified Scale for the Assessment of Neg. Symptoms (SANS) summary scores, and to compare efficacy and tolerability opposite placebo and haloperidol. Three hundred sixty-one patients from 26 North American centers entered this double-blind, placebo-controlled trial with acute exacerbation of chronic schizophrenia (DSM-III-R). Patients who completed a single-blind, placebo washout phase were randomized to double-blind treatment with quetiapine (75, 150, 300, 600, or 750 mg daily), haloperidol (12 mg daily), or placebo and evaluated weekly for 6 wk. At end point, significant differences ($p < 0.05$, anal. of covariance) in adjusted mean changes from baseline were identified between the four highest doses of quetiapine and placebo for BPRS total, BPRS pos.-symptom cluster, and CGI Severity of Illness item scores and between quetiapine 300 mg and placebo for SANS summary score. Differences between quetiapine and haloperidol were not significant. Dose-response modeling showed significant linear and quadratic functions of quetiapine dose for all primary efficacy variables. Notably, no significant safety concerns were identified as dose increased. Quetiapine was no different from placebo across the dose range studied regarding incidence of extrapyramidal symptoms or change in prolactin concns. Quetiapine is well tolerated and clin. effective in the treatment of schizophrenia. It is both superior to placebo and comparable to haloperidol in reducing pos. symptoms at doses ranging from 150 to 750 mg/day and in reducing neg. symptoms at a dose of 300 mg/day.

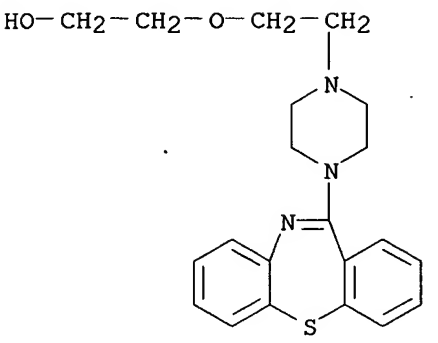
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(multiple fixed doses of quetiapine in patients with acute exacerbation of schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

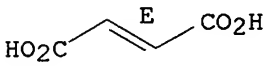
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 70 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:511843 CAPLUS
DOCUMENT NUMBER: 127:117369
TITLE: Method of predicting a subjects response to neuroleptic agents
INVENTOR(S): Royston, Maureen Claire
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK; Royston, Maureen Claire
SOURCE: PCT Int. Appl., 13 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9721833	A1	19970619	WO 1996-EP5734	19961211
W: AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CU, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IL, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, TJ, TM, TR, TT, UA, UG, US, UZ, VN, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, ML, MR, NE, SN, TD, TG				
AU 9713762	A1	19970703	AU 1997-13762	19961211
ZA 9610458	A	19980612	ZA 1996-10458	19961212
PRIORITY APPLN. INFO.:			GB 1995-25481 A	19951213
			WO 1996-EP5734 W	19961211

AB A method of assessing in a subject the likelihood whether said subject will be non-responsive or responsive to treatment with a drug the primary mode of action of which is via a process of altered synaptic activity, the method comprising detecting the presence or absence of DNA comprising the E2 allele of the ApoE gene, or of protein expressed by said DNA, in a biol. sample obtained from said subject. The method is exemplified with an atypical neuroleptic agent, i.e. clozapine.

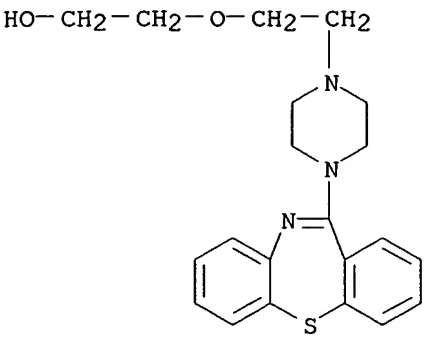
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(drug therapy of schizophrenia and detection of E2 allele of the ApoE gene for prediction of therapeutic outcome)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

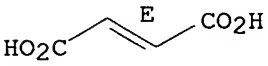
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 71 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:457442 CAPLUS
DOCUMENT NUMBER: 127:171462
TITLE: [35S]Guanosine-5'-O-(3-thio)triphosphate binding as a measure of efficacy at human recombinant dopamine D4.4 receptors: actions of antiparkinsonian and antipsychotic agents
AUTHOR(S): Newman-Tancredi, A.; Audinot, V.; Chaput, C.; Verriele, L.; Millan, M. J.
CORPORATE SOURCE: Dep. of Psychopharmacology, Institut de Recherches Servier, Croissy-sur-Seine, 78290, Fr.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1997), 282(1), 181-191
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Recombinant human dopamine D4.4 receptor-mediated G protein activation was characterized in membranes of transfected mammalian (Chinese hamster ovary) cells by the use of [35S]guanosine-5'-O-(3-thio)triphosphate ([35S]GTPγS) binding. An initial series of expts. defined the conditions (3 μM GDP, 100 mM NaCl, 3 mM MgCl2) under which optimal stimulation (2.2-fold increase in specific [35S]GTPγS binding) was achieved with the endogenous agonist dopamine. The number of dopamine-activated G proteins in Chinese hamster ovary-D4.4 membranes was determined through [35S]GTPγS isotopic dilution saturation binding, yielding a Bmax value of 2.29 pmol/mg. This compared with a D4.4 receptor Bmax value of 1.40 pmol/mg determined by [3H]spiperone saturation binding, indicating that 1 or 2 G proteins were activated per D4.4 receptor and that there were few or no "spare receptors" in this cell line. Under these conditions, the efficacy for stimulation of [35S]GTPγS binding at D4.4 receptors of 12 dopaminergic agonists was determined Several antiparkinsonian drugs, including ropinirole, quinerolane and lisuride, exhibited agonist activity at D4.4 receptors (Emax = 74.3%, 72.4% and 32.2%, resp., compared with dopamine = 100%). The EC50 values for agonist stimulation of [35S]GTPγS binding correlated well with the inhibition consts. derived from competition binding with [3H]spiperone (r = +.99). However, other antiparkinsonian drugs (bromocriptine, L-DOPA and terguride) showed low affinity and/or were devoid of agonist activity at D4.4 receptors. The potency at D4.4 receptors of the novel, selective D4.4 receptor antagonist L 745,870 was determined, indicting that it has high affinity (Ki = 1.99 nM) without detectable agonist activity. Furthermore, L 745,870 completely inhibited dopamine-stimulated [35S]GTPγS binding with a Kb value of 1.07 nM. The action of an addnl. 20 chemical diverse dopaminergic ligands, including clozapine, ziprasidone, sertindole, olanzapine and several other "atypical" antipsychotics, in advanced development was investigated. Each of these ligands shifted the dopamine stimulation curve to the right in a parallel manner consistent with competitive antagonism at this site and yielding Kb values (32.6, 22.4, 17.2 and 26.5 nM, resp.) that agreed closely with their Ki values (38.0, 14.9, 18.5 and 26.1 nM). In contrast, raclopride and seroquel exhibited low affinity at D4.4 receptors (Ki > 1000 nM). Other compds. that showed antagonist activity at D4.4 receptors included the 5-hydroxytryptamine2A receptor antagonist fananserin (RP 62203), the sigma ligand BMY 14,802 and the D3 receptor antagonist GR 103,691. In conclusion, dopamine D4.4 receptor activity is unlikely to be an important factor in the clin. effectiveness of antiparkinsonian drugs, although low agonist efficacy at D4.4 receptors might be associated with a lesser incidence of side effects. Furthermore, antagonist activity at D4.4 receptors is a common property of many typical and atypical antipsychotic agents.

QUETIAPINE

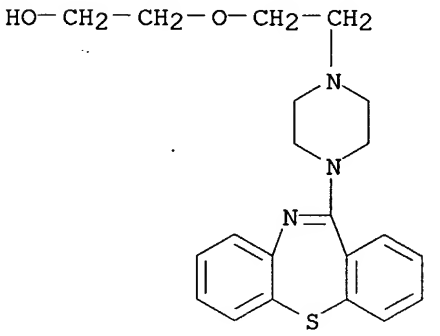
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(guanosine-5'-O-(3-thio)triphosphate binding as measure of efficacy at human dopamine D4 receptors: actions of antiparkinsonian and antipsychotic agents)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

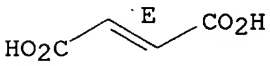
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 72 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:241193 CAPLUS
DOCUMENT NUMBER: 126:287593
TITLE: Modeling of neuroleptics with and without EPS side effects
AUTHOR(S): Lien, Eric J.; Das, Arima; Lien, Linda l.
CORPORATE SOURCE: Dep. Pharm. Sciences, Univ. Southern California, Los Angeles, CA, 90033, USA
SOURCE: Chinese Pharmaceutical Journal (Taipei) (1996), 48(5), 387-396
CODEN: CPHJEP
PUBLISHER: Pharmaceutical Society of Republic of China
DOCUMENT TYPE: Journal
LANGUAGE: English

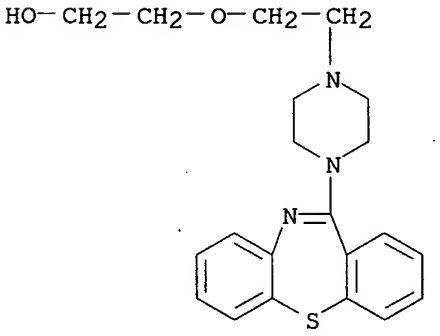
AB Mol. modeling with HyperChem program is used to more accurately measure the interplanar angle of the hydrophobic ring system, as well as the dipole moment of selected neuroleptics for comparison. After geometry optimization and energy minimization, the interplanar angle between the two benzene rings in chlorpromazine is found to be 155°, while that in the atypical neuroleptic without EPS side effect, i.e., clozapine, is 125°. For the newer neuroleptics with minimal EPS side effects, the interplanar angles lie in between, 135° for olanzapine and 145° for seroquel. All of the neuroleptics posses a pos.-charged nitrogen atom under physiol. condition. For most of them it is separated from a ring system by a distance of three carbon atoms or its equivalent The dipole moments of the uncharged species (2.16-4.59 D), while important, do not appear to be the determining factor for EPS side effects.

IT **111974-72-2**, Seroquel.
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(modeling of neuroleptics with and without EPS side effects)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

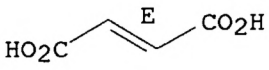


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



QUETIAPINE

L26 ANSWER 73 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:196129 CAPLUS
DOCUMENT NUMBER: 126:259004
TITLE: Muscarinic m4 receptor activation by some atypical antipsychotic drugs
AUTHOR(S): Zeng, Xiang Ping; Le, Fei; Richelson, Elliott
CORPORATE SOURCE: Mayo Foundation Medical Education Res., Mayo Clinic, Jacksonville, FL, 32224, USA
SOURCE: European Journal of Pharmacology (1997), 321(3), 349-354
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB To clarify the findings that clozapine is both a muscarinic receptor agonist and antagonist, the authors examined the effects of neuroleptics on forskolin-stimulated cAMP accumulation in Chinese hamster ovary cells expressing human muscarinic m4 receptors (CHO-hm4) and in rat striatum. With CHO-hm4 cells, clozapine induced a concentration-dependent and atropine-sensitive inhibition on cAMP formation, with EC5o = 60 mM and Emax = 74% of carbachol maximum Other atypical neuroleptics, fluperlapine, tenilapine and olanzapine, were similar but less potent, while risperidone, rilapine, quetiapine (ICI 204,636), sertindole, and ziprasidone had almost no effect. Typical neuroleptics, haloperidol, chlorpromazine, fluphenazine, thiothixene, thioridazine, and molindone, showed either no effect or an atropine-resistant inhibition of cAMP formation. However, in rat striatal tissues, clozapine, up to 10 μM, did not show a significant inhibition of cAMP formation, probably due to a relatively low abundance of muscarinic m4 receptors and the presence of multiple types of muscarinic and other receptors, with which clozapine interacts. Nevertheless, muscarinic m4 receptor agonism, to some, extent, may be a relevant mechanism for the therapeutic efficacy and side effects of clozapine and some atypical neuroleptics.

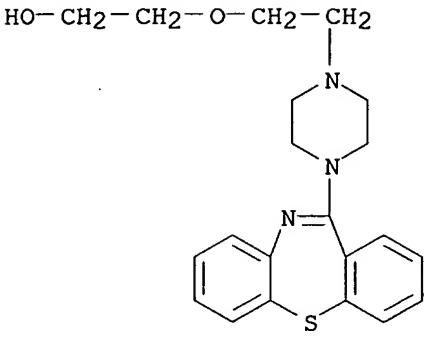
IT **111974-72-2**, ICI204636
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(muscarinic m4 receptor activation by atypical antipsychotic drugs in Chinese hamster ovary cells and rat striatum)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

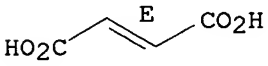
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 74 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:48321 CAPLUS
DOCUMENT NUMBER: 126:99217
TITLE: Endogenous dopamine limits the binding of antipsychotic drugs to D3 receptors in the rat brain: A quantitative autoradiographic study
AUTHOR(S): Schotte, A.; Janssen, P. F. M.; Bonaventure, P.; Leysen, J. E.
CORPORATE SOURCE: Department Biochemical Pharmacology, Janssen Research Foundation, Beerse, B-2340, Belg.
SOURCE: Histochemical Journal (1996), 28(11), 791-799
CODEN: HISJAE; ISSN: 0018-2214
PUBLISHER: Chapman & Hall
DOCUMENT TYPE: Journal
LANGUAGE: English

AB [3H]7-hydroxy-N,N-di-n-propyl-2-aminotetralin was used as a radioligand for the autoradiog. measurements of dopamine D3 receptors in rat and human brain. Preincubation of the brain sections was necessary to obtain binding of the radioligand in the islands of Calleja and in the nucleus accumbens, but not in cerebellar lobules 9/10 of the rat. D3 receptors were also totally occluded in unwashed sections of the human striatum. The radioligand binding to D3 receptors was maximal after preincubating the sections for at least 10 min. Pretreatment of the animals with reserpine or tetrabenazine, which results in a severe depletion of endogenous monoamines, strongly reduces the occlusion of D3 receptors in unwashed brain sections. The occlusion of dopamine D3 receptors in brain sections suggests that the in vivo access to D3 receptors may be locally inhibited by endogenous dopamine. The in vitro binding affinities of 12 antipsychotic drugs for D2 and D3 receptors were evaluated in competition binding expts., using both rat and cloned human receptors. Most of the compds. showed only a slightly lower affinity for D3 than for D2 receptors in vitro. Affinities of the antipsychotic drugs for cloned human D2L and D3 receptors were very close to their affinities for the rat receptors. In vivo occupancy of these receptors in the rat brain was measured ex vivo by quant. autoradiog., 2 h after s.c. drug administration. For most compds., occupancy of D3 receptors, as compared to D2 receptor occupancy, was lower than expected from the corresponding in vivo affinity ratios. For the new antipsychotic risperidone, in vivo occupancy of D3 receptors was measured both in the islands of Calleja and in the cerebellar lobules 9/10. This compound was three times less potent for the occupancy of D3 receptors in the islands of Calleja than in the cerebellum, an area lacking endogenous dopamine (ED50 = 28 and 10 mg kg-1, resp.). Based on the observations in the rat brain, it may reasonably be supposed that therapeutic dosages of antipsychotic drugs will induce in patients only a minor occupancy of D3 receptors in brain areas containing high dopamine concns. The role of dopamine D3 receptors as a target of antipsychotic drugs may therefore be less important than previously thought.

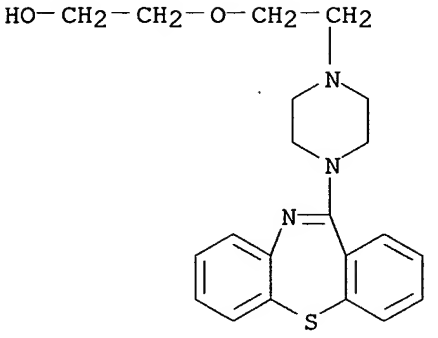
IT **111974-72-2**, Seroquel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(endogenous dopamine limits binding of antipsychotic drugs to D3 receptors in rat brain: a quant. autoradiog. study)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

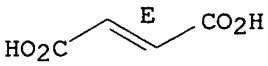
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



REFERENCE COUNT: 25 THERE ARE 25 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

QUETIAPINE

L26 ANSWER 75 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1997:6767 CAPLUS
DOCUMENT NUMBER: 126:84470
TITLE: Seroquel restores sensorimotor gating in phencyclidine-treated rats
AUTHOR(S): Swerdlow, Neal R.; Bakshi, Vaishali; Geyer, Mark A.
CORPORATE SOURCE: Dep. of Psychiatry and Neurosciences Program, Univ. of California, San Diego, La Jolla, CA, 2093-0804, USA
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1996), 279(3), 1290-1299
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Phencyclidine (PCP) is a psychotomimetic noncompetitive glutamate antagonist that has been used in studies of the neural substrates of psychosis. Both schizophrenic patients and PCP-treated rats exhibit reduced amts. of prepulse inhibition (PPI) of the startle reflex, which is the normal inhibition of startle that occurs when the startling noise is preceded 30 to 500 ms by a weak prepulse. The present study assessed the effects of seroquel (ICI 204,636), a mixed D2/5-hydroxytryptamine2 antagonist with a preclin. profile suggestive of potential antipsychotic efficacy, on the PCP-induced disruption of PPI. Clozapine, risperidone and haloperidol were also studied as comparison compds. PCP (1.25 mg/kg) significantly reduced PPI, with prepulses that were 1 to 12 dB above background. Seroquel and clozapine significantly restored PPI in PCP-treated rats, whereas haloperidol and risperidone did not. Similar findings were obtained in studies using sep. animals, a slightly lower dose of PCP (1.0 mg/kg) and a high dose of each of these antipsychotics. Sep. studies verified that risperidone and haloperidol restored PPI in apomorphine-treated rats. In the present studies, seroquel exhibited a profile consistent with those exhibited by other "atypical" antipsychotics.

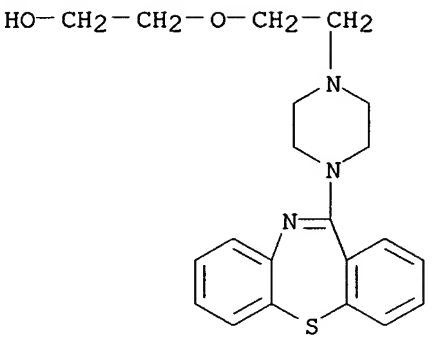
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(seroquel restores sensorimotor gating in phencyclidine-treated rats in relation to antipsychotic activity)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

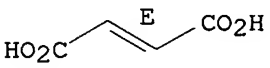
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



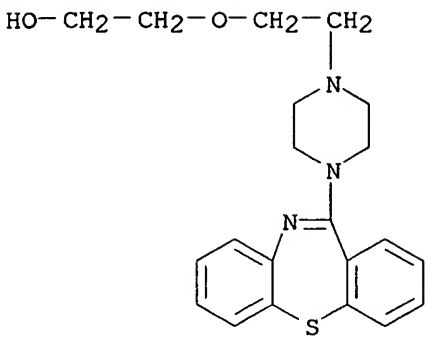
QUETIAPINE

L26 ANSWER 76 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:750480 CAPLUS
DOCUMENT NUMBER: 126:70003
TITLE: Iloperidone binding to human and rat dopamine and 5-HT receptors
AUTHOR(S): Kongsamut, Sathapana; Roehr, Joachim E.; Cai, Jidong; Hartman, Harold B.; Weissensee, Paul; Kerman, Lisa L.; Tang, Lei; Sandrasagra, Anthony
CORPORATE SOURCE: Neuroscience Research, Hoechst Marion Roussel, Inc., Route 202-206, P.O. Box 6800, Bridgewater, NJ, 08807-0800, USA
SOURCE: European Journal of Pharmacology (1996), 317(2/3), 417-423
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English
AB Iloperidone (HP 873; 1-[4-[3-[4-(6-fluoro-1,2-benzisoxazol-3-yl)-1-piperidinyl]propoxy]-3-methoxyphenyl]ethanone) is a compound currently in clin. trials for the treatment of schizophrenia. Iloperidone displays affinity for dopamine D2 receptors and for 5-HT2A receptors and has a variety of in vivo activities suggestive of an atypical antipsychotic. Here we present an examination of the affinity of iloperidone to a variety of human and rat homologs of dopamine and 5-HT receptor subtypes. We employed receptor binding assays using membranes from cells stably expressing human dopamine D1, D2S, D2L, D3, D4 and D5 and 5-HT2A and 5-HT2C receptors and rat 5-HT6 and 5-HT7 receptors. Iloperidone displayed higher affinity for the dopamine D3 receptor (Ki = 7.1 nM) than for the dopamine D4 receptor (Ki = 25 nM). Iloperidone displayed high affinity for the 5-HT6 and 5-HT7 receptors (Ki = 42.7 and 21.6 nM, resp.), and was found to have higher affinity for the 5-HT2A (Ki = 5.6 nM) than for the 5-HT2C receptor (Ki = 42.8 nM). The potential implications of this receptor binding profile are discussed in comparison with data for other antipsychotic compds.
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); PROC (Process); USES (Uses)
(binding of iloperidone and other antipsychotic drugs to human and rat dopamine and 5-HT receptors)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

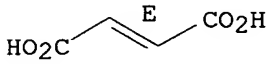
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 77 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:713012 CAPLUS
DOCUMENT NUMBER: 125:317310
TITLE: Method for determining the responsiveness of individuals to 5-HT2 receptor-modulating agents
INVENTOR(S): Kerwin, Robert; Collier, David; Roberts, Gareth Wyn
PATENT ASSIGNEE(S): Smithkline Beecham Plc, UK
SOURCE: PCT Int. Appl., 15 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
WO 9631621	A2	19961010	WO 1996-EP1437	19960401
WO 9631621	A3	19961205		
W: AL, AM, AT, AU, AZ, BB, BG, BR, BY, CA, CH, CN, CZ, DE, DK, EE, ES, FI, GB, GE, HU, IS, JP, KE, KG, KP, KR, KZ, LK, LR, LS, LT, LU, LV, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI				
RW: KE, LS, MW, SD, SZ, UG, AT, BE, CH, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN				
AU 9654991	A1	19961023	AU 1996-54991	19960401
JP 11503018	T2	19990323	JP 1996-529970	19960401
ZA 9602716	A	19970122	ZA 1996-2716	19960404
PRIORITY APPLN. INFO.:			GB 1995-7230 A	19950407
			WO 1996-EP1437 W	19960401

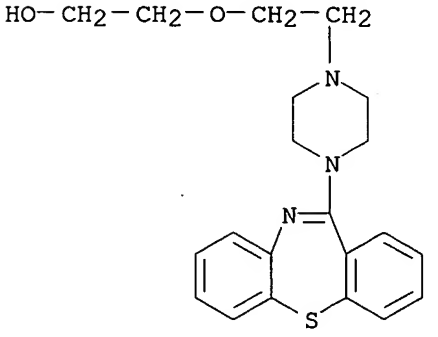
AB A method is disclosed for assessing whether a subject is likely to be responsive to treatment with a therapeutic agent which acts at a 5-HT2 receptor. The methodol. involves detection of the presence or absence of DNA encoding the S68 allele and/or the C68 allele of the 5-HT2C gene.

IT **111974-72-2**, Seroquel
RL: THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(C68/S68 allele of 5-HT2C gene detection in 5-HT2 receptor-modulating agent responsiveness determination for humans treatable with 5-HT2 receptor-modulating agents)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

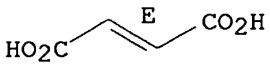
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 78 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:638479 CAPLUS
DOCUMENT NUMBER: 125:292824
TITLE: Activity of "Seroquel" (ICI 204,636) in animal models for atypical properties of antipsychotics: A comparison with clozapine
AUTHOR(S): Ellenbroek, Bart A.; Lubbers, Luuk J.; Cools, Alexander R.
CORPORATE SOURCE: Department Psychoneuropharmacology, University Nijmegen, Nijmegen, 6500 HB, Neth.
SOURCE: Neuropsychopharmacology (1996), 15(4), 406-416
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

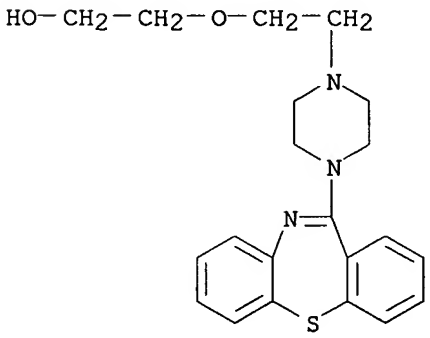
AB The pharmacol. treatment of schizophrenia still suffers from two major problems: (1) most antipsychotic drugs still induce severe neurol. (extrapyramidal) side effects; (2) few antipsychotic drugs are effective in treating the neg. symptoms of schizophrenia. In the present study, we have evaluated the effects of ICI 204,636 in the rat paw test and the amphetamine-induced social isolation in monkeys and compared them with the effects of clozapine. The paw test has been shown to be a valid model for differentiating classic and atypical neuroleptic drugs. The monkey social isolation model seems to represent one of the few animal models with validity for the neg. symptoms of schizophrenia. The results show that both ICI 204,636 and clozapine had the profile of an atypical antipsychotic in the paw test, suggesting a reduced propensity to induce extrapyramidal side effects in humans. Likewise, ICI 204,636 and clozapine were found to prevent the amphetamine-induced social isolation in monkeys, suggesting a good therapeutic effect mitigating the neg. symptoms in schizophrenia. Overall, the data suggest that ICI 204,636 may represent a new and interesting antipsychotic drug, closely resembling clozapine.

IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(atypical antipsychotic Seroquel and treatment of schizophrenia)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

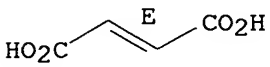


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 79 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:486829 CAPLUS
DOCUMENT NUMBER: 125:157462
TITLE: 'Seroquel' (quetiapine): preclinical and clinical findings of a new atypical antipsychotic
AUTHOR(S): Casey, Daniel E.
CORPORATE SOURCE: VA Medical Center, Portland, OR, USA
SOURCE: Expert Opinion on Investigational Drugs (1996), 5(8), 939-957
CODEN: EOIDER; ISSN: 0967-8298
PUBLISHER: Ashley Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review with .apprx.45 refs. This article first briefly reviews the preclin. of 'Seroquel' (quetiapine, Zeneca Pharmaceuticals), a novel dibenzothiazepine antipsychotic agent in late-stage clin. development, especially with respect to its potential as an atypical antipsychotic with a pharmacol. profile similar to clozapine, but without the significant side-effects associated with clozapine. The rest of the article is a detailed review of the clin. studies of quetiapien completed to date. These include three placebo-controlled studies (Studies 4, 6, and (8)), one open-labeled study (Study (5)), and one study in which quetiapine was compared to chlorpromazine (Study (7)). Details of the study designs and the efficacy, safety, and tolerability analyses are provided, and a summary of the results of each study is presented. Based on the findings in these five studies, quetiapine appears to be an effective antipsychotic agent for the treatment of both the pos. and neg. symptoms of schizophrenia, with efficacy that is statistically significantly superior to placebo and comparable to chlorpromazine. Quetiapine causes few extrapyramidal symptoms or acute dystonic reactions (rates are similar to placebo across the dose range), and it does not produce sustained elevations in serum prolactin. The clin. distinguish quetiapine from standard antipsychotics and further support its designation as an atypical antipsychotic.

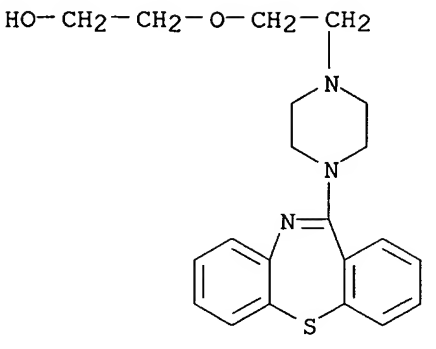
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
('Seroquel' (quetiapine) dealing with preclin. and clin. findings of a new atypical antipsychotic in humans)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

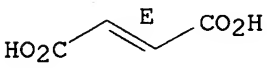
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 80 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:426705 CAPLUS
DOCUMENT NUMBER: 125:104943
TITLE: Plasma prolactin in schizophrenia subjects treated with Seroquel (ICI 204,636)
AUTHOR(S): Hamner, Mark B.; Arvanitis, Lisa A.; Miller, Barbara G.; Link, Christopher G. G.; Hong, Walter W.
CORPORATE SOURCE: Department Psychiatry, Medical University South Carolina, Charleston, SC, USA
SOURCE: Psychopharmacology Bulletin (1996), 32(1), 107-110
CODEN: PSYBB9; ISSN: 0048-5764
PUBLISHER: U.S. Dep. of Health and Human Services
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Treatment with standard antipsychotic medications causes side effects such as hyperprolactinemia and extrapyramidal symptoms. Because these side effects can cause noncompliance with antipsychotic medication and consequent relapse, they add to the morbidity of schizophrenia. A compound with antipsychotic efficacy but without the side effects of standard antipsychotic agents would improve compliance and treatment outcomes and enhance quality of life. Improved compliance, reduced relapse, and decreased hospitalization would also reduce the cost of treatment of schizophrenia. Seroquel (ICI 204,636), an atypical antipsychotic compound in Phase III development, was found to be well tolerated and effective in treating subjects with DSM-III-R schizophrenia in three Phase II clin. trials. Anal. of plasma prolactin concns. obtained during these trials revealed that ICI 204,636 did not differ from placebo in its effect on plasma prolactin after up to 6 wk of treatment; no significant difference was found in the degree of decline of plasma prolactin levels when subjects treated with ICI 204,636 and placebo were compared. A significant difference was found, however, between ICI 204,636- and chlorpromazine-treated subjects; prolactin levels in ICI 204,636-treated subjects fell to a greater degree than they did in chlorpromazine-treated subjects, however in all three trials, ICI 204,636 did not cause sustained elevation of prolactin.

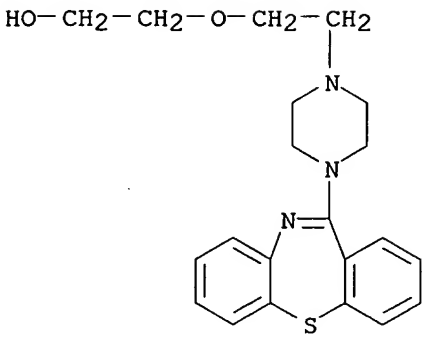
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(plasma prolactin in schizophrenia subjects treated with Seroquel (ICI 204,636))

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

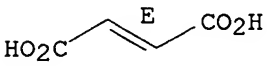
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 81 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:355773 CAPLUS
DOCUMENT NUMBER: 125:49068
TITLE: Differential effect of antipsychotics on place navigation of rats in the Morris water maze. A comparative study between novel and reference antipsychotics
AUTHOR(S): Skarsfeldt, T.
CORPORATE SOURCE: H. Lundbeck A/S, Copenhagen-Valby, DK-2500, Den.
SOURCE: Psychopharmacology (Berlin) (1996), 124(1/2), 126-133
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

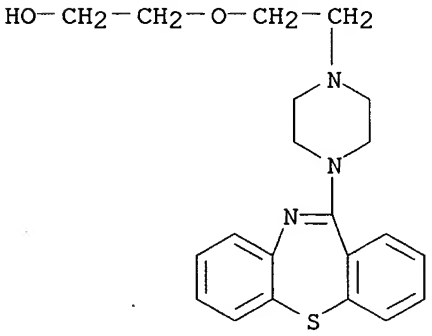
AB A group of novel neuroleptics (e.g. olanzapine, seroquel, sertindole and ziprasidone) and already marketed compds. (e.g. clopazine, haloperidol and risperidone) were tested for acute effect on spatial learning and memory in Morris' water maze task. Young rats were trained for 4 consecutive days (three trials/day) to find a platform situated beneath the water surface. Two compds., sertindole and seroquel, were without effect on spatial performance, whereas clozapine impaired performance on the first 2 test days but showed no effect compared to the controls on the last 2 test days. Ziprasidone and olanzapine markedly impaired spatial memory without affecting motor function (measured by the swimming speed). Risperidone and haloperidol also impaired performance but in addition both compds. significantly lowered the swimming speed. The present study indicates that several of the compds. impair spatial learning in Morris water maze. This might be of clin. importance in the treatment of schizophrenics, as many of these patients already show severe cognitive deficits. Therefore, certain antipsychotics could worsen the pre-existing memory deficits in schizophrenic patients and this aspect should be considered before antipsychotic treatment.

IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BIOL (Biological study)
(differential effect of novel and reference antipsychotics on spatial learning and memory in relation to schizophrenia treatment)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

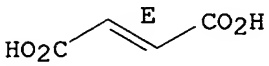


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 82 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:355772 CAPLUS
DOCUMENT NUMBER: 125:49067
TITLE: Inhibitory effects on the discriminative stimulus properties of D-amphetamine by classical and newer antipsychotics do not correlate with antipsychotic activity. Relation to effects on the reward system?
AUTHOR(S): Arnt, J.
CORPORATE SOURCE: H. Lundbeck A/S, Copenhagen-Valby, DK-2500, Den.
SOURCE: Psychopharmacology (Berlin) (1996), 124(1/2), 117-125
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Classical antipsychotics exemplified by haloperidol (0.30), fluphenazine (0.070) and cis(Z)-flupentixol (0.088; ED50 values in μmol/kg are given in parentheses for all compds.) potently block the discriminative stimulus properties of D-amphetamine (1.0 mg/kg, IP) in rats. Newer antipsychotics have very different profiles: clozapine (7.2) and olanzapine (5.9) induce dose-dependent inhibition, while risperidone (>6.1) and remoxipride (>47) show weak inhibitory effects and sertindole (>23), seroquel (>20), amperozide (2.9) and the putative antipsychotic MDL 100151 (>13; racemate with MDL 100907 as the active enantiomer) are ineffective. Antagonists of α1-adrenoceptors (prazosin; >6.0), 5-HT2A/2C (ritanserin; >2.6) and histamine H1 receptors (mepyramine; >50) are ineffective. Sertindole (0.076), risperidone (0.23), clozapine (0.39), olanzapine (0.088), MDL 100151 (0.0082), fluphenazine (0.13) and ritanserin (0.12) are potent inhibitors of the discriminative stimulus induced by the 5-HT2A/2c agonist DOI (0.63 mg/kg, IP), while haloperidol (.apprx.0.4), cis(Z)-flupentixol(.apprx.0.04), amperozide (0.5) and prazosin (>12) show partial inhibition and remoxipride (>23) and mepyramine (>25) are ineffective. The results indicate that inhibition of D-amphetamine discrimination does not correlate with antipsychotic activity of new antipsychotics, as has previously been suggested in the literature. Furthermore, the inhibitory potencies against D-amphetamine-induced discrimination (present study) and hypermotility (previous study in the same strain of rats do not correlate either for several of the newer antipsychotics (e.g. for sertindole, risperidone, seroquel and remoxipride). The discrepancies cannot solely be explained by addnl. pharmacol. effects of these compds., e.g. 5-HT2 receptor blockade. The D-amphetamine discrimination is documented to depend on increased limbic dopamine function which in humans is associated with increased euphoria. Based on these results, it is hypothesized that D-amphetamine discrimination rather than a model for antipsychotic activity may reflect dysphoric or anhedonic activity.

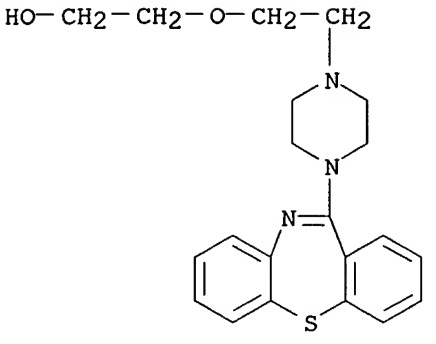
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(D-amphetamine discrimination does not correlate with antipsychotic activity of new antipsychotics)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

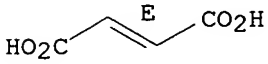
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 83 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:355767 CAPLUS
DOCUMENT NUMBER: 125:49064
TITLE: Risperidone compared with new and reference antipsychotic drugs: in vitro and in vivo receptor binding
AUTHOR(S): Schotte, A.; Janssen, P. F. M.; Gommeren, W.; Luyte, W. H. M. L.; Van Gompel, P.; Lesage, A. S.; De Loore, K.; Leysen, J. E.
CORPORATE SOURCE: Dep. Biochem. Pharmacol., Janssen Res. Found., Beerse, B-2340, Belg.
SOURCE: Psychopharmacology (Berlin) (1996), 124(1/2), 57-73
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Risperidone and its active metabolite 9-OH-risperidone were compared to reference antipsychotic drugs (haloperidol, pipamperone, fluspirilene, clozapine, zotepine) and compds. under development (olanzapine, seroquel, sertindole, ORG-5222, ziprasidone) for in vitro binding to neurotransmitter receptors in brain tissue and on membranes of recombinant cells expressing cloned human receptors and for in vivo occupancy of neurotransmitter receptors in rat and guinea-pig brain following acute treatment (2 h, s.c.). An ex vivo autoradiog. technique was applied to determine the receptor occupancy by the drugs administered in vivo. Of particular interest are the central 5HT2A receptors and D2-type receptors. Predominant 5HT2A receptor antagonism is supposed to add to an atypical profile of the antipsychotics (treatment of the neg. symptoms, low incidence of extrapyramidal side effects). D2 antagonism is required for the treatment of a pos. symptoms. A contribution of the new dopamine receptor subtypes D3 and in particular D4 receptors has been proposed. In vitro, all compds., except the 'typical' antipsychotics haloperidol and fluspirilene, showed higher affinity for 5HT2A than for D2 receptors. Subnanomolar affinity for human 5HT2A receptors was observed for ORG-5222, sertindole, risperidone, 9-OH-risperidone and zotepine displayed nanomolar affinity for human D2 receptors. Sertindole and olanzapine were slightly less potent. Pipamperone, clozapine and seroquel showed 2 orders of magnitude lower D2 affinity in vitro. Clozapine, but even more so pipamperone, displayed higher affinity for D4 than for D2 receptors. For most other compds., D4 affinity was only slightly lower than their D2 affinity. Seroquel was totally devoid of D4 affinity. None of the compds. had nanomolar affinity for D1 receptors; their affinity for D3 receptors was usually slightly lower than for D2 receptors. In vivo, ORG-5222, risperidone, pipamperone, 9-OH-risperidone, sertindole, olanzapine, zotepine and clozapine maintained a higher potency for occupying 5HT2A than D2 receptors. Risperidone and ORG-5222 had 5HT2A vs. D2 potency ratio of about 20. Highest potency for 5HT2A receptor occupancy was observed for ORG-5222 followed by risperidone and olanzapine. Ziprasidone exclusively occupied 5HT2/A receptors. No regional selectivity for D2 receptor occupancy in mesolimbic vs. nigrostriatal areas was detected for any of the test compds. Risperidone was conspicuous because of its more gradual occupancy of D2 receptors; none of the other compds. showed this property. The various compds. also displayed high to moderate occupancy of adrenergic α1 receptors, except fluspirilene and ziprasidone. Clozapine, zotepine, ORG-5222 and sertindole occupied even more α1 than D2 receptors. Clozapine showed predominant occupancy of H1 receptors and occupied cholinergic receptors with equivalent potency to D2 receptors. A stronger predominance of 5HT2A vs. D2 receptor occupancy combined with a more gradual occupancy of D2 receptors differentiates risperidone and its 9-OH-metabolite from the other antipsychotic compds. in this study. The predominant 5HT2A receptor

occupancy probably plays a role in the beneficial action of risperidone on the neg. symptoms of schizophrenia, whereas maintenance of a moderate occupancy of D2 receptors seems adequate for treating the pos. symptoms of schizophrenia. A combined 5HT2A and D2 occupancy and the avoidance of D2 receptor overblockade are believed to reduce the risk for extrapyramidal symptoms.

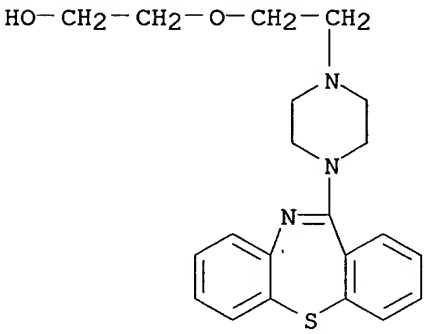
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(risperidone compared with new and reference antipsychotic drugs)

RN 111974-72-2 CAPLUS

CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

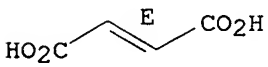
CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 84 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:355765 CAPLUS
DOCUMENT NUMBER: 125:49062
TITLE: Comparison of the new atypical antipsychotics olanzapine and ICI 204,636 with clozapine on behavioral responses to the selective "D1-like" dopamine receptor agonist A 68930 and selective "D2-like" agonist RU 24213
AUTHOR(S): Deveney, A. M.; Waddington, J. L.
CORPORATE SOURCE: Dep. Clin. Pharmacol., R. Coll. Surgeons, Dublin, Ire.
SOURCE: Psychopharmacology (Berlin) (1996), 124(1/2), 40-49
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The effects of the putative atypical antipsychotics olanzapine and ICI 204,636 on behavioral responses to the selective "D2-like" dopamine receptor agonist RU 24213 and to the selective "D1-like" agonist A 68930 were compared with those of the prototype atypical antipsychotic clozapine, the selective D1-like antagonist SCH 23390 and the selective D2-like antagonist YM 09151-2. Olanzapine (0.4-2.0 mg/kg) and ICI 204,636 (4.0-36.0 mg/kg), like clozapine (4.0-36.0 mg/kg) and SCH 23390 (0.01-1.0 mg/kg), effected at best modest reduction in typical sniffing and locomotor responses and, with the exception of ICI 204,636, released episodes of atypical myoclonic jerking to RU 24213 (12.5 mg/kg); a high dose of olanzapine (10.0 mg/kg), like YM 09151-2 (0.005-0.5 mg/kg), blocked all responsivity to RU 24213. Conversely, olanzapine (0.4-2.0 mg/kg) and ICI 204,636 (4.0-36.0 mg/kg), like clozapine (4.0-12.0 mg/kg) and SCH 23390 (0.01-0.1 mg/kg), readily blocked typical grooming responses to A 68930 (0.5 mg/kg); YM 09151-2 failed to block grooming and exerted more variable effects. Olanzapine and, to a lesser extent, ICI 204,636 share with clozapine a preferential action to attenuate D1-mediated function; given their lack of selectivity affinity for D1-like receptors, this common effect may be exerted at an alternative level of synaptic function. The action of olanzapine and particularly ICI 204,636 to release addnl. episodes of atypical vacuous chewing to A 68930 indicates some deviation from a wholly clozapine-like profile, the clin. significance of which remains to be specified.

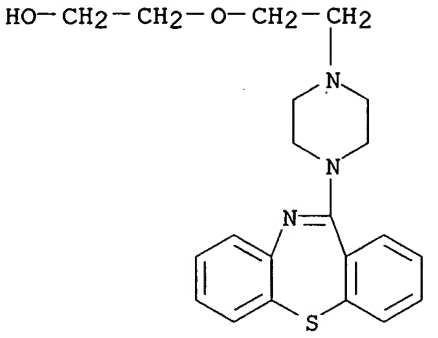
IT **111974-72-2**, ICI 204636
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(atypical antipsychotics olanzapine and ICI 204636 effect mediation by dopamine receptors: comparison with clozapine)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

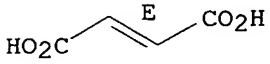
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 85 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1996:138439 CAPLUS
DOCUMENT NUMBER: 124:250583
TITLE: Radioreceptor binding profile of the atypical antipsychotic olanzapine
AUTHOR(S): Bymaster, Frank P.; Calligaro, David O.; Falcone, Julie F.; Marsh, Richard D.; Moore, Nicholas A.; Tye, Nicholas C.; Seeman, Philip; Wong, David T.
CORPORATE SOURCE: Lilly Research Laboratories, Lilly Corporate Center, Indianapolis, IN, 46285, USA
SOURCE: Neuropsychopharmacology (1996), 14(2), 87-96
CODEN: NEROEW; ISSN: 0893-133X
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

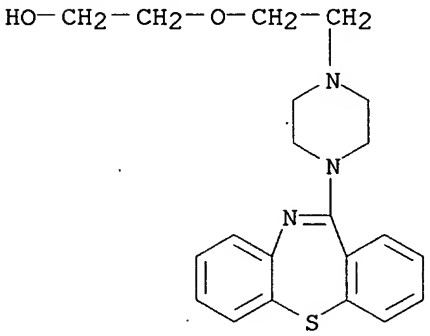
AB The affinities of olanzapine, clozapine, haloperidol, and four potential antipsychotics were compared on binding to the neuronal receptors of a number of neurotransmitters. In both rat tissues and cell lines transfected with human receptors olanzapine had high affinity for dopamine D1, D2, D4, serotonin (5HT)2A, 5HT2C, 5HT3, α1-adrenergic, histamine H1, and five muscarinic receptor subtypes. Olanzapine had lower affinity for α2-adrenergic receptors and relatively low affinity for 5HT1 subtypes, GABAA, β-adrenergic receptors, and benzodiazepine binding sites. The receptor binding affinities for olanzapine was quite similar in tissues from rat and human brain. The binding profile of olanzapine was comparable to the atypical antipsychotic clozapine, while the binding profiles for haloperidol, risperidone, remoxipride, Org 5222, and seroquel were substantially different from that of clozapine. The receptor binding profile of olanzapine is consistent with the antidopaminergic, antiserotonergic, and antimuscarinic activity observed in animal models and predicts atypical antipsychotic activity in man.

IT **111974-72-2**, Seroquel
RL: BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(radioreceptor binding profile of atypical antipsychotic olanzapine and other antipsychotics)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

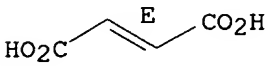


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 86 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:894259 CAPLUS
DOCUMENT NUMBER: 123:328978
TITLE: Pre-clinical pharmacology of ICI 204,636
AUTHOR(S): Goldstein, J. M.; Takeshita, Takashi; Iswaran, T. J.
CORPORATE SOURCE: Zeneca Pharm., Wilmington, DE, 19850-5437, USA
SOURCE: Shinkei Seishin Yakuri (1995), 17(10), 683-92
CODEN: SSYAD7; ISSN: 0388-7588
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review with 27 refs. on affinity of antipsychotic ICI 204,636 to cerebral receptors, its effect on behavior, its electrophysiol., and prediction of psychotropic agent-induced extrapyramidal symptoms.

IT **111974-72-2**, ICI 204636
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BPR (Biological process); BSU (Biological study, unclassified); BIOL (Biological study); PROC (Process)
(pharmacol. of antipsychotic ICI 204,636)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

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CRN 111974-69-7
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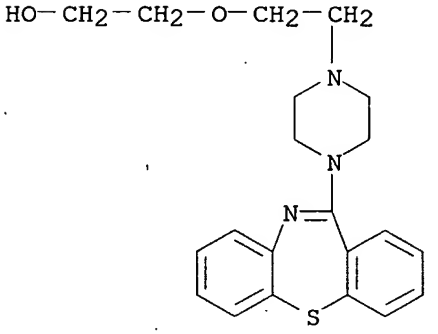

CM 2

CRN 110-17-8
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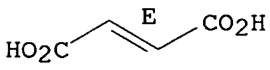
Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 87 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:859498 CAPLUS
DOCUMENT NUMBER: 123:329010
TITLE: ICI 204,636 (Seroquel): A dibenzothiazepine atypical antipsychotic. review of preclinical pharmacology and highlights of phase II clinical trials
AUTHOR(S): Goldstein, Jeffrey M.; Arvanitis, Lisa A.
CORPORATE SOURCE: CNS Biomedical Research, ZENECA Pharmaceuticals, Wilmington, DE, 19850-5437, USA
SOURCE: CNS Drug Reviews (1995), 1(1), 50-73
CODEN: CDREFB; ISSN: 1080-563X
PUBLISHER: Neva Press
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
AB A review with 42 refs. on preclin. pharmacol. and phase II clin. trials of Seroquel (ICI 204,636).
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(preclin. pharmacol. and phase II clin. trials of dibenzothiazepine atypical antipsychotic Seroquel (ICI 204,636) in humans)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
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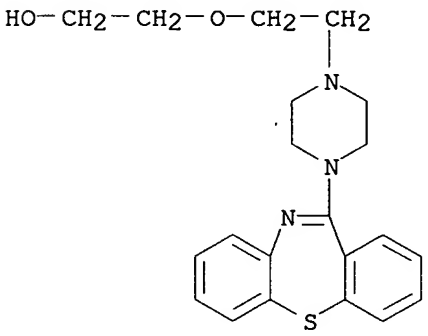

CM 2

CRN 110-17-8
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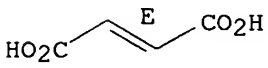
Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 88 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:809376 CAPLUS
DOCUMENT NUMBER: 123:246661
TITLE: D4 dopamine receptor binding affinity does not distinguish between typical and atypical antipsychotic drugs
AUTHOR(S): Roth, B. L.; Tandra, S.; Burgess, L. H.; Sibley, D. R.; Meltzer, H. Y.
CORPORATE SOURCE: Sch. Med., Case Western Reserve Univ., Cleveland, OH, 44106-4935, USA
SOURCE: Psychopharmacology (Berlin) (1995), 120(3), 365-8
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

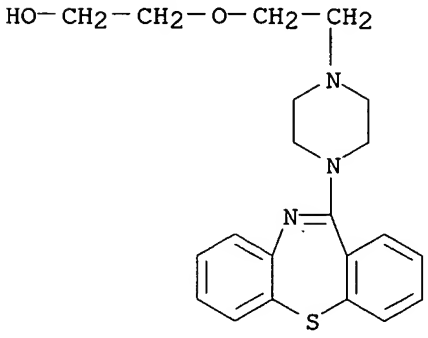
AB The affinities of 13 atypical and 12 typical antipsychotic drugs for the cloned rat D4 dopamine receptor and the D4/D2 ratios were examined Of the atypical antipsychotic drugs tested, only clozapine, risperidone, olanzapine, zotepine and tiospirone had affinities less than 20 nM. In fact, many atypical antipsychotic drugs had relatively low affinities for the cloned rat D4 receptor, with Ki values greater than 100 nM (Seroquel, fluperlapine, tenilapine, FG5803 and melperone). Addnl., several typical antipsychotic drugs had high affinities for the cloned rat D4 receptor, with Kis less than 20 nM (loxapine, chlorpromazine, fluphenazine, mesoridazine, thioridazine and trifluoroperazine). The ratios of D2/D4 affinities did not differentiate between these two types of antipsychotic drugs. Thus, D4 dopamine receptor affinity, used as a single measure, does not distinguish between the group of typical and atypical antipsychotic drugs analyzed.

IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(D4 dopamine receptor binding affinity of typical and atypical antipsychotic drugs)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

QUETIAPINE

CRN 110-17-8
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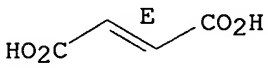


QUETIAPINE

L26 ANSWER 89 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:791199 CAPLUS
DOCUMENT NUMBER: 123:275719
TITLE: Differential effects of classical and newer antipsychotics on the hypermotility induced by two dose levels of D-amphetamine
AUTHOR(S): Arnt, Jorn
CORPORATE SOURCE: Pharmacological Research, H. Lundbeck A/S, Ottiliavej 9, Copenhagen-Valby, DK-2500, Den.
SOURCE: European Journal of Pharmacology (1995), 283(1-3), 55-62
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The inhibitory effects of a variety of established and putative antipsychotic compds. on the hypermotility induced by D-amphetamine at two dose levels (0.5 and 2.0 mg/kg) have been studied. Classical antipsychotics (haloperidol, fluphenazine and cis(Z)-flupentixol) and the selective dopamine D2 receptor antagonist remoxipride inhibit hypermotility in the two conditions with similar potencies, whereas sertindole, clozapine, risperidone, ziprasidone and olanzapine preferentially inhibit the effect of the low dose of D-amphetamine (selectivity ratios between 6.5 and 18). Seroquel, amperozide and the selective 5-HT2A receptor antagonist MDL 100.151 ((±)-α-(2,3-dimethoxyphenyl)-1-[2-(4-fluorophenylethyl)]-4-piperidine-m ethanol) have no effect on D-amphetamine 2.0 mg/kg, but inhibit the response to D-amphetamine 0.5 mg/kg. The α1-adrenoceptor antagonist prazosin inhibits the motility response to D-amphetamine 0.5 mg/kg with slightly higher potency than that to D-amphetamine 2.0 mg/kg, whereas the 5-HT2A/2C receptor antagonist ritanserin selectively inhibits the effect of D-amphetamine 0.5 mg/kg. The histamine H1 receptor antagonist mepyramine is ineffective in both models. All compds., except remoxipride, MDL 100.151 and ritanserin (which are ineffective) inhibit spontaneous locomotor activity at dose levels close to those inhibiting the response to D-amphetamine 2.0 mg/kg. Prazosin has partial inhibitory effect. In conclusion, dopamine antagonism has similar inhibitory effect on hyperactivity induced by low and high D-amphetamine dosages, α1-adrenoceptor antagonism also contributes to both effects, whereas 5-HT2 receptor antagonism selectively interacts with the low D-amphetamine dose. This indicates that the responses to D-amphetamine 0.5 and 2.0 mg/kg are differently modulated by these neurotransmitters. These results indicate that the dose level of D-amphetamine inducing hyperactivity is important for the pharmacol. of this response and indicate that different neuronal interactions are involved. The implications of these observations for the improved ratio between efficacy and neurol. side-effects of newer antipsychotics are discussed.

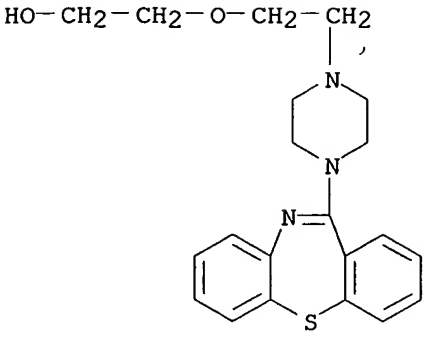
IT **111974-72-2**, Seroquel
RL: ADV (Adverse effect, including toxicity); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(differential effects of classical and newer antipsychotics on the hypermotility induced by two dose levels of D-amphetamine)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

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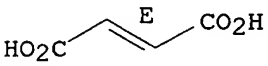


QUETIAPINE

L26 ANSWER 90 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:751427 CAPLUS
DOCUMENT NUMBER: 123:188329
TITLE: Differential effects of repeated administration of novel antipsychotic drugs on the activity of midbrain dopamine neurons in the rat
AUTHOR(S): Skarsfeldt, Torben
CORPORATE SOURCE: Pharmacological Research, Research and Development, H. Lundbeck A/S, Ottiliavej 9, Copenhagen-Valby, DK-2500, Den.
SOURCE: European Journal of Pharmacology (1995), 281(3), 289-94
CODEN: EJPHAZ; ISSN: 0014-2999
PUBLISHER: Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

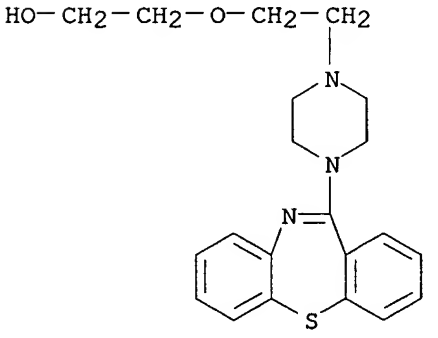
AB Five potential antipsychotics (i.e. risperidone, olanzapine, seroquel, ziprasidone and amperozide) were given daily for 21 days to rats and the effect on the number of spontaneously active dopamine neurons in ventral tegmental area and substantia nigra pars compacta was determined Standard electrophysiol. measurements (i.e. single unit recording technique) were used. Risperidone, olanzapine and amperozide showed some selectivity (at one particular dose) for decreasing the number of active dopamine neurons in the ventral tegmental area. However, risperidone induced a U-shaped dose-response curve. The highest dose of amperozide inhibited the activity in substantia nigra pars compacta, showing a liability to induce extrapyramidal side-effects. Seroquel and ziprasidone inhibited the activity in both areas indicating a classical antipsychotic profile (i.e. high liability to cause extrapyramidal side-effects).

IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(effects of antipsychotic drugs on midbrain dopamine neuronal activity in rats)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

QUETIAPINE

CRN 110-17-8
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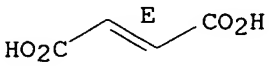
Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 91 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:644818 CAPLUS
DOCUMENT NUMBER: 123:47775
TITLE: Seroquel (ICI 204 636), a putative "atypical" antipsychotic, in schizophrenia with positive symptomatology: results of an open clinical trial and changes of neuroendocrinological and EEG parameters
AUTHOR(S): Wetzel, H.; Szegedi, A.; Hain, Ch.; Wiesner, J.; Schlegel, S.; Benkert, O.
CORPORATE SOURCE: Dept. Psychiatry, Univ. Mainz, Mainz, D-55131, Germany
SOURCE: Psychopharmacology (Berlin) (1995), 119(2), 231-8
CODEN: PSCHDL; ISSN: 0033-3158
PUBLISHER: Springer
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Preclin. data indicated that seroquel (ICI 204 636), a dibenzothiazepine with 5-HT2 and D2-like receptor antagonistic properties, might be an effective antipsychotic agent, causing fewer extrapyramidal side effects than typical neuroleptics. In the present study, 12 patients suffering from schizophrenia or schizophreniform disorder with predominantly pos. symptomatol. were treated in an open clin. trial for 4 wk with seroquel at a maximum dosage of 750 mg/day. The drug was generally well tolerated, and virtually no adverse extrapyramidal side effects such as acute dystonia, parkinsonism or akathisia were observed Total scores for BPRS (item score 0-6; base-line: 42.0), SAPS (64.5) and SANS (55.0) showed a moderate decrease at the end of treatment (BPRS: 30.0; SAPS: 36.1; SANS: 42.5), when intention-to-treat anal. was applied. There were considerable interindividual differences in treatment response, with some subjects showing almost full remission of pos. symptoms, in contrast to about half of the patients who showed no satisfactory clin. improvement. Interestingly, patients showing good antipsychotic response reported slight initial side effects like mild sedation. Prolactin and TSH levels were not altered during seroquel administration. As to pharmaco-EEG investigations, seroquel caused a moderate increase of the absolute power in the alpha, theta, and beta frequency bands, paralleled by a decrease of delta activity. There were no signs of paroxysmal EEG activity under seroquel. Our results suggest that seroquel may be a well tolerated drug with some antipsychotic properties, exhibiting no extrapyramidal side effects that could be of use in the treatment of schizophrenic patients with pos. symptomatol. Further double-blind studies with higher doses, to test presumably better efficacy, and with monitoring of plasma levels, are needed to extend the present results.

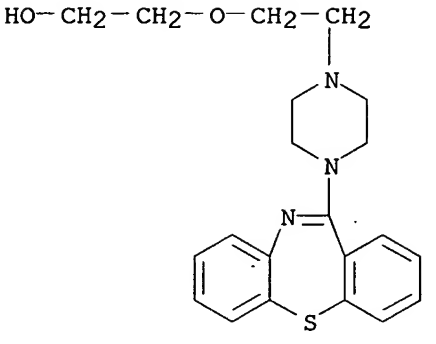
IT **111974-72-2**, Seroquel
RL: BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(antipsychotic seroquel treatment of schizophrenia and absence of extrapyramidal side effects)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

QUETIAPINE



CM 2

CRN 110-17-8
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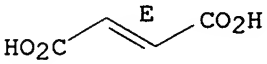
Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 92 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1995:248026 CAPLUS
DOCUMENT NUMBER: 122:46284
TITLE: Induction patterns of Fos-like immunoreactivity in the forebrain as predictors of atypical antipsychotic activity
AUTHOR(S): Robertson, George S.; Matsumura, Hiroko; Fibiger, Hans C.
CORPORATE SOURCE: Fac. Med., Univ. Ottawa, Ottawa, K1H 8M5, Can.
SOURCE: Journal of Pharmacology and Experimental Therapeutics (1994), 271(2), 1058-66
CODEN: JPETAB; ISSN: 0022-3565
PUBLISHER: Williams & Wilkins
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Clozapine and haloperidol produce different induction patterns of c-fos expression in the forebrain, with haloperidol increasing Fos-like immunoreactivity (FLI) in the striatum, nucleus accumbens, lateral septal nucleus and clozapine producing such effects in the nucleus accumbens, prefrontal cortex and lateral septal nucleus. Accordingly, it was deemed possible that this approach may be useful in characterizing compds. with known or suggested antipsychotic actions. We therefore examined the effects of 17 compds. considered to be either typical, or atypical, antipsychotics on FLI in the prefrontal cortex, medial and dorsolateral striatum, nucleus accumbens and the lateral septal nucleus. Consistent with the hypothesis that the prefrontal cortex may be a target for some antipsychotic actions, FLI was elevated in this structure by clozapine, ICI 204,636, fluperlapine, RMI-81,582, remoxipride, molindone, melperone and tiospirone. Likewise, the ability of all of the compds., except for risperidone, to enhance FLI in the lateral septal nucleus suggests that this limbic region also may be an important locus of antipsychotic action. All of the compds. examined elevated FLI in the nucleus accumbens and medial striatum, indicating that potential antipsychotic activity is predicted most consistently on this basis. Neuroleptics with a clearly documented liability for producing extrapyramidal side effects (EPS) such as chlorpromazine, fluphenazine, haloperidol, loxapine, metoclopramide and molindone elevated FLI in the dorsolateral striatum. In contrast, compds. unlikely to produce EPS such as clozapine, thioridazine, risperidone, remoxipride, fluperlapine, sulpiride, melperone and RMI-81,582 either failed to increase or produced minor elevations in FLI in the dorsolateral striatum. Hence, the ability of a neuroleptic to increase FLI in the dorsolateral striatum predicted reasonably well its propensity to induce EPS. However, in order to devise a more precise classification scheme, we compared the difference between the number of neurons which displayed neuroleptic-induced FLI in the nucleus accumbens vs. that in the dorsolateral striatum after administration of each of the 17 compds. This difference, referred to as the atypical index, was always pos. for atypical antipsychotics and invariably neg. for typical neuroleptics. Thus, in every instance it was possible to accurately predict the potential for EPS on the basis of whether the atypical index was pos. or neg. These results suggest that Fos immunohistochem. is a rapid and reliable method for determining the EPS liability of potential antipsychotic agents.

IT **111974-72-2**, ICI 204636
RL: ADV (Adverse effect, including toxicity); BAC (Biological activity or effector, except adverse); BSU (Biological study, unclassified); BIOL (Biological study)
(Fos-like immunoreactivity patterns in the forebrain as predictors of atypical antipsychotic activity and extrapyramidal effects)

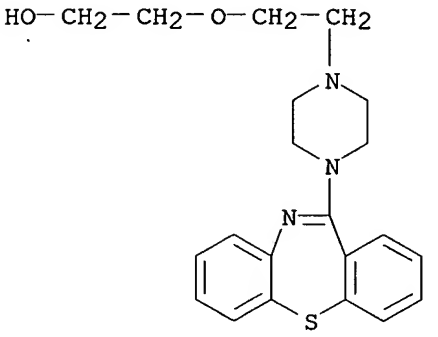
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-,

QUETIAPINE

(2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

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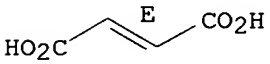


QUETIAPINE

L26 ANSWER 93 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:449989 CAPLUS
DOCUMENT NUMBER: 121:49989
TITLE: Seroquel (ICI 204,636) restores prepulse inhibition of acoustic startle in apomorphine-treated rats: similarities to clozapine
AUTHOR(S): Swerdlow, Neal R.; Zisook, Daniel; Taaid, Navid
CORPORATE SOURCE: Sch. Med., UCSD, La Jolla, CA, 92093-0804, USA
SOURCE: Psychopharmacology (Berlin) (1994), 114(4), 675-8
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

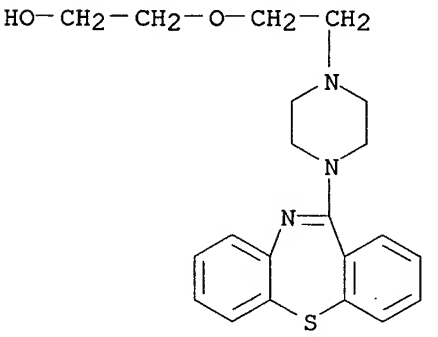
AB Seroquel (ICI 204,636) is a mixed D2/5HT2 antagonist with a preclin. profile suggestive of potential antipsychotic efficacy. The authors compared seroquel to clozapine in an animal model of sensorimotor gating deficits in schizophrenic patients. Like schizophrenic patients, rats treated with apomorphine (APO) exhibit deficits in prepulse inhibition (PPI) of acoustic startle. The ability of antipsychotics to restore PPI in APO-treated rats correlates (Rs = 0.991) with their clin. potency. Seroquel and clozapine both restore PPI and APO-treated rats. Seroquel's restoration of PPI in apomorphine-treated rats follows simple monotonic ascending dose-response properties, and is not accompanied by consistent changes in startle reflex amplitude. Seroquel's profile in this PPI model mimics that of other antipsychotics.

IT **111974-72-2**, Seroquel
RL: BIOL (Biological study)
(sensorimotor gating deficit therapy with)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

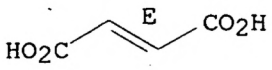


CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.

QUETIAPINE



QUETIAPINE

L26 ANSWER 94 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:461 CAPLUS
DOCUMENT NUMBER: 120:461
TITLE: Seroquel: Behavioral effects in conventional and novel tests for atypical antipsychotic drug
AUTHOR(S): Migler, Bernard M.; Warawa, Edward J.; Malick, Jeffrey B.
CORPORATE SOURCE: Dep. Chem., ICI Americas Inc., Wilmington, DE, 19897, USA
SOURCE: Psychopharmacology (Berlin, Germany) (1993), 112(2-3), 299-307
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

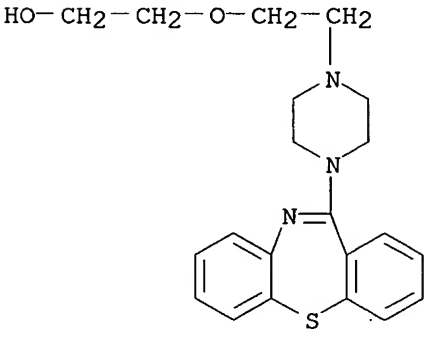
AB Seroquel was compared to clozapine and several other antipsychotic agents in tests predictive of antipsychotic activity or extrapyramidal symptoms. In the conditioned avoidance test in squirrel monkeys as well as several paradigms using apomorphine or amphetamine-induced behavioral alterations, seroquel displayed the profile of a drug with potential antipsychotic activity. In these paradigms the potency of seroquel was somewhat less than clozapine in rodent tests, while the reverse was true in higher species, i.e. monkeys, cats. In tests designed to evaluate the propensity to induce EPS or tardive dyskinesia, for example, the production of dyskinetic reactions in haloperidol-sensitized cebus monkeys, seroquel displayed a profile similar to clozapine and disparate from typical antipsychotic drugs. In drug-naive cebus monkeys seroquel sensitized significantly fewer monkeys than haloperidol and the dyskinetic reactions were of significantly less intensity. It is anticipated that this novel antipsychotic agent will have a significantly reduced propensity to produce extrapyramidal symptoms and tardive dyskinesia than typical antipsychotics.

IT **111974-72-2**, Seroquel
RL: BIOL (Biological study)
(antipsychotic, behavioral effects of, extrapyramidal symptoms in relation to)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

QUETIAPINE

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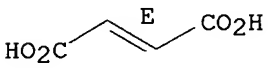


QUETIAPINE

L26 ANSWER 95 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:460 CAPLUS
DOCUMENT NUMBER: 120:460
TITLE: Seroquel: Electrophysiological profile of a potential atypical antipsychotic
AUTHOR(S): Goldstein, Jeffrey M.; Litwin, Linda C.; Sutton, Evelynjean B.; Malick, Jeffrey B.
CORPORATE SOURCE: Dep. Pharmacol., ICI Americas Inc., Wilmington, DE, 19897, USA
SOURCE: Psychopharmacology (Berlin, Germany) (1993), 112(2-3), 293-8
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

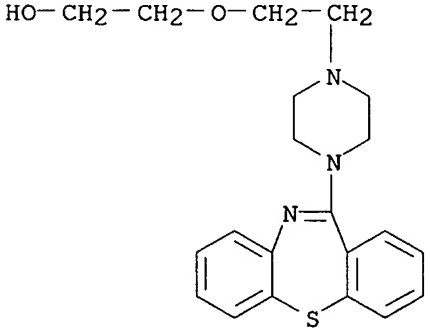
AB Extracellular single unit recording techniques were employed to compare the effects of seroquel with the reference antipsychotic (AP) agents clozapine and haloperidol in electrophysiol. tests that may predict AP activity. Seroquel and clozapine were differentially more active in reversing the inhibitory actions of d-amphetamine on mesolimbic (A10) than nigrostriatal (A9) dopamine (DA)-containing neurons, whereas haloperidol exhibited the opposite selectivity. In cell population studies, acute treatment with seroquel and clozapine selectivity increased the number of spontaneously active A10 DA cells, which was found to correlate with the ability of both these drugs to cause depolarization inactivation (DI) of A10 DA cells following repeated (28 day) administration. This profile of activity was unlike that of haloperidol, which acutely caused a nonselective increase in the number of active A9 and A10 DA cells, associated with the ability of this agent to cause DI of both A9 and A10 DA cells after repeated treatment. Since DI of A10 DA cells may be correlated with AP efficacy whereas DI of A9 DA cells may predict the ability of an APto cause extrapyramidal side effects (EPS) and tardive dyskinesia (TD), seroquel, like clozapine, may be an atypical AP with a reduced likelihood for producing EPS/TD.

IT **111974-72-2**, Seroquel
RL: BIOL (Biological study)
(antipsychotic, brain dopaminergic system response to, extrapyramidal side effects and tardive dyskinesia in relation to)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

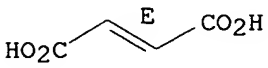


QUETIAPINE

CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 96 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1994:459 CAPLUS
DOCUMENT NUMBER: 120:459
TITLE: Seroquel: Biochemical profile of a potential atypical antipsychotic
AUTHOR(S): Saller, Charles F.; Salama, Andre I.
CORPORATE SOURCE: Dep. Pharmacol., Zeneca Pharm. Group, Wilmington, DE, 19897, USA
SOURCE: Psychopharmacology (Berlin, Germany) (1993), 112(2-3), 285-92
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Seroquel and the atypical antipsychotic clozapine were compared using a number of biochem. measures in rats which are indicative of potential antipsychotic activity and possible extrapyramidal side effect liability. Both in vitro and in vivo, these compds. are low potency D-2 dopamine (DA) receptor antagonists and are relatively more potent 5-HT2 antagonists than typical antipsychotic drugs. Seroquel also exhibited low affinity for D-1 DA receptors in vitro, but D-1 receptor occupancy was not detectable in vivo. Unlike clozapine, seroquel lacks appreciable activity at either D-1 DA or muscarinic receptors. Following i.p. administration, both compds. produce similar elevations in DA metabolite concns. Following 1 mo of daily administration, at doses which produce large increases in striatal DA metabolite concns., both seroquel and clozapine fail, unlike typical antipsychotics, to increase the number of striatal D-2 receptors, but do decrease the number of 5-HT2 receptors in frontal cortex. ICI 204,636 produces a short-lasting increase in plasma prolactin levels, but these increases are much greater than those that are produced by clozapine. One day after 3 wk of daily administration, tolerance to the ability of seroquel to elevate DA metabolite and plasma PRL concns. is not observed These biochem. observations are discussed with regard to the atypical profile of seroquel in behavioral and electrophysiol. studies.

IT **111974-72-2**, Seroquel
RL: BIOL (Biological study)
(antipsychotic, biochem. profile of)

RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
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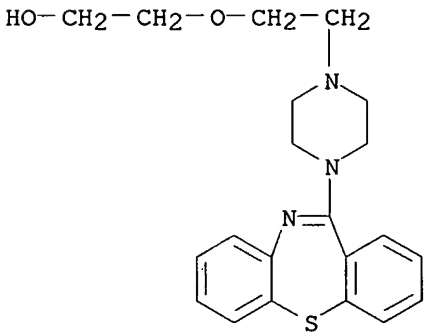
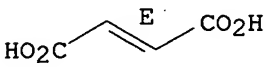


QUETIAPINE

CM 2

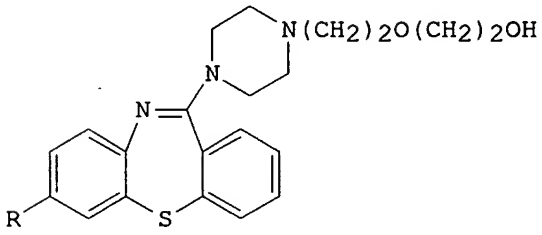
CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 97 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1992:98783 CAPLUS
DOCUMENT NUMBER: 116:98783
TITLE: Determination of an antipsychotic agent (ICI 204,636) and its 7-hydroxy metabolite in human plasma by high-performance liquid chromatography and gas chromatography-mass spectrometry
AUTHOR(S): Pullen, Robert H.; Palermo, Karen M.; Curtis, Michael A.
CORPORATE SOURCE: Drug Dispos. Metabl. Dep., ICI Am. Inc., Wilmington, DE, 19897, USA
SOURCE: Journal of Chromatography (1992), 573(1), 49-57
CODEN: JOCRAM; ISSN: 0021-9673
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, R=H
II, R=OH

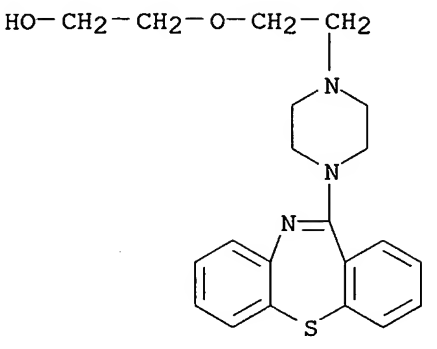
AB ICI 204,636 (I) is an orally active antipsychotic agent under development for the treatment of schizophrenia in humans. It is partially converted in animals to an active 7-hydroxy metabolite (II). Methods were developed for the simultaneous determination of both analytes in human plasma using high-performance liquid chromatog. (HPLC) and gas chromatog.-mass spectrometry (GC-MS). The analytes were extracted from plasma using Ph solid-phase extraction columns. Quantification by isocratic HPLC was performed in the reversed-phase mode with detection at 250 nm. Exts. were derivatized to trimethylsilyl ethers for quantification by GC-MS using selected-ion monitoring. Both assays were evaluated for consistency of response, precision, accuracy and specificity. Limits of quantification for I and II by HPLC were 15 and 20 ng/mL, resp.; limits of quantification for I and II by GC-MS were 2 and 5 ng/mL, resp. Both methods were applied to the anal. of clin. samples from oral dosing studies with I.

IT **111974-72-2**
RL: ANT (Analyte); ANST (Analytical study)
(determination of, in blood of humans, by GC and HPLC)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S

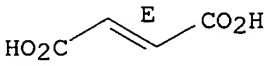
QUETIAPINE



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.



QUETIAPINE

L26 ANSWER 98 OF 98 CAPLUS COPYRIGHT 2005 ACS on STN
ACCESSION NUMBER: 1991:199539 CAPLUS
DOCUMENT NUMBER: 114:199539
TITLE: Selective antidopaminergic effects of S-(+)-N-n-propylnoraporphines in limbic versus extrapyramidal sites in rat brain: comparisons with typical and atypical antipsychotic agents
AUTHOR(S): Campbell, Alexander; Yeghiayan, Sylva; Baldessarini, Ross J.; Neumeyer, John L.
CORPORATE SOURCE: Dep. Psychiatry, Harvard Med. Sch., Boston, MA, USA
SOURCE: Psychopharmacology (Berlin, Germany) (1991), 103(3), 323-9
CODEN: PSCHDL; ISSN: 0033-3158
DOCUMENT TYPE: Journal
LANGUAGE: English

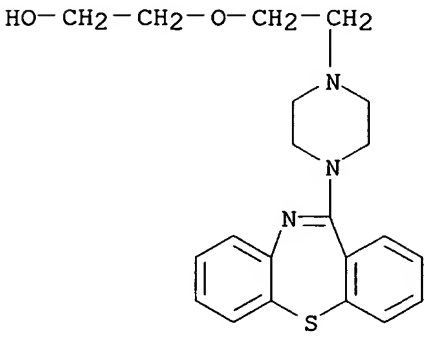
AB Dopamine (DA), injected unilaterally into rat forebrain after pretreatment with a monoamine oxidase inhibitor, equipotently induced locomotor arousal when placed in the nucleus accumbens septi (a limbic site) and contralateral deviation of the head when placed in the corpus striatum (an extrapyramidal target); testing was done with an ED50 dose of DA (16 μg). Systemic injections (i.p.) of the representative typical neuroleptic haloperidol showed high potency and minor striatal selectivity against the behavioral effects of intracerebral DA [accumbens ID50 = 0.090, striatum = 0.027 mg/kg (0.24 and 0.072 μmol/kg); ID50 ratio = 3.3, favoring striatum]. The atypical antipsychotic agent clozapine was less potent against DA in both brain regions but, paradoxically, showed ever greater striatal selectivity [ID50 = 12 and 1.4 mg/kg (37 and 4.2 μmol/kg); ratio = 8.8, favoring striatum], while its analog, the piperazinyl-dibenzothiazepine ICI-204,636 showed intermediate potency and the lowest striatal selectivity of these three neuroleptic agents [ID50 = 1.8 and 0.88 mg/kg (4.1 and 2.0 μmol/kg); ratio = 2.1]. In striking contrast, the S(+) isomers of N-n-propylnorapomorphine, its orally active 10,11-methylenedioxy prodrug derivative, and its 11-monohydroxy analog all induced potent antagonism of limbic DA but had little effect on extrapyramidal injections of DA except at high systemic doses [ID50, accumbens = 0.18-0.52, striatal = 10-15 mg/kg (0.50-1.6 and 29-42 μmol/kg); regional ID50 ratios = 18-69, favoring accumbens]. The S(+)-aporphines showed limbic potency similar to that of haloperidol and 25-73 times greater than that of clozapine. The S-(+)-11-OH-aporphine was 2.7-3.1 times more potent (on a molar dose basis) than the other aporphines against DA in accumbens, and 0.5, 8, and 73 times as potent as haloperidol, ICI-204,636, and clozapine. The significantly dissimilar slopes of dose-effect functions for the two groups of agents suggest that different actions may mediate the limbic effects of the aporphines and the neuroleptics tested. ICI-204-636 appears to be pharmacol. similar to clozapine, but 2.1 times more potent vs. limbic-DA. The S-(+)-N-n-propylnoraporphines are potent and regionally highly selective limbic DA antagonists and S-(+)-11-hydroxy-N-n-propylnoraporphine is orally active. These and other aporphine analogs are proposed for development as potential atypical antipsychotic agents with a low risk of extrapyramidal neurol. side effects, and the present methods are proposed for predicting relative limbic vs. extrapyramidal antidopaminergic activity.

IT **111974-72-2**, ICI 204636
RL: BIOL (Biological study)
(dopaminergic-antagonist activity of, in brain extrapyramidal vs. limbic system, antipsychotic activity in relation to)
RN 111974-72-2 CAPLUS
CN Ethanol, 2-[2-(4-dibenzo[b,f][1,4]thiazepin-11-yl-1-piperazinyl)ethoxy]-, (2E)-2-butenedioate (2:1) (salt) (9CI) (CA INDEX NAME)

QUETIAPINE

CM 1

CRN 111974-69-7
CMF C21 H25 N3 O2 S



CM 2

CRN 110-17-8
CMF C4 H4 O4

Double bond geometry as shown.